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Beijing and Hangzhou, China
1-14 November 1982

Technical papers

Part One**

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**Part Two, containing further technical papers, will be circulated under the symbol UNIDO/IO.615.

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Preface

The papers presented in this volume were originally given at the Workshop on the Pharmaceutical Industry (Combined Modern and Traditional Pharmacy) for Promoting Technical Co-operation among Developing Countries held in Beijing and Hangzhou, 1 to 14 November 1982.

Jointly organized by the Government of the People's Republic of China and the United Nations Industrial Development Organization (UNIDO), the workshop was held so that other developing countries could benefit from the Chinese experience in developing a methodology for utilizing available ethnomedical information as a guide to enriching health care systems.

The lectures enabled meeting participants to understand the philosophy underlying Chinese traditional medicine and to appreciate what research and development has gone into building a scientific basis around traditional medicine.

In this context the meeting recognized that there is considerable scope for enhanced co-operation between China and other developing countries particularly in the area of plant drug supply.

Specific recommendations from the meeting participants included:

(a) Establishing a joint UNIDO/China programme to facilitate co-operation between China and other developing countries;

(b) Selective translation of Chinese literature and texts as an aid to technical co-operation and collaboration;

(c) Collation and dissemination of information on available Chinese technology for production of plant-derived pharmaceuticals, active natural products and their analogues;

(d) Action to enable other developing countries to benefit directly from Chinese expertise in areas of assessment of medical plant resources, agronomic aspects of plant cultivation, pharmacological screening of plant species for medical use, technologies for processing drugs whose efficacy and safety have been validated, methodologies for producing simplified preparations from prescriptions used in traditional medicine, design and layout of production-scale manufacturing plant and maintenance of product quality.

The meeting also recommended that the formal presentations be published in a single volume as the proceedings of the meeting. The following pages therefore include seven papers presented by Chinese experts and one contribution from UNIDO.

CONTENTS

Page

Preface 2

AN INTRODUCTION TO CHINESE MATERIA MEDICA
Shen Jiaxiang 5

BASIC CONCEPTS OF CHINESE TRADITIONAL MEDICINE
Xie Zhufan 29

CLINICAL APPLICATIONS OF TRADITIONAL AND HERBAL DRUGS
Li Shun Cheng 37

MODERN RESEARCH ON CHINESE TRADITIONAL AND HERBAL DRUGS
Xiao Peigen 47

TRADITIONAL CHINESE DOSAGE FORMS AND THEIR MODERNIZATION
Hu Changhong 59

DEVELOPMENTS IN INDUSTRIAL PRODUCTION OF CHINESE TRADITIONAL AND HERBAL REMEDIES
Liu Deyan 73

STANDARDIZATION OF CHINESE MATERIA MEDICA
Lou Zhi-cen 85

TRADITIONAL PHARMACOPOEIAS REVISITED
UNIDO secretariat 95

AN INTRODUCTION TO CHINESE MATERIA MEDICA

By Shen Jiaxiang*

A B S T R A C T

The Chinese materia medica is defined as consisting of traditional drugs, herbal drugs and minority drugs. Both classical and contemporary works on Chinese materia medica are surveyed to show historical developments. Basic concepts in classical medical theories such as the life composition and the understanding of the body's interior are discussed with reference to classical philosophical background. The classical pharmacology and pharmacological classification of drugs are briefly presented. The evidence presented shows that it is the therapeutic effectiveness of a drug that dictates the assignment of its pharmacological category.

Occidental materia medica and Graeco-Roman concepts of pharmacology are compared. The prospect for Chinese materia medica are viewed in the light of Western medical history.

Chinese materia medica

Chinese materia medica comprise traditional drugs, herbal drugs and drugs used by minority groups.

Specifically, the term Chinese traditional drugs (Zhong-yao) refers only to drugs used in accordance with the guidelines of traditional medicine. Usually they go into recipes; seldom are they used alone. Thus, in Chinese traditional medicine, Herba ephedrae (Ma-huang) is a principal ingredient in a variety of formulations intended to exert diaphoretic, anti-asthmatic, as well as diuretic action. Of these, diaphoresis is the most important. Because of this, we could not regard ephedrine as its true active principle. Ephedrine in fact is employed in modern therapy in a quite different way. Another example is glycyrrhiza (liquorice), which has long been used in both Chinese and Western medicine. In Western medicine it was used earlier as an emollient and in recent years has been found to be active against peptic ulcers and Addison's disease. But in Chinese traditional medicine Radix glycyrrhizae (Gan-cao) has been accorded a very general role in a wide variety of formulations. Apart from being a tonic for the digestive tract and an emollient for the pulmonary orb (lungs), it is regarded as a universal detoxicant and is used in recipes as a master mediator of different drug actions. It is this application profile that defines glycyrrhiza as a Chinese traditional drug.

The designation "herbal drugs" is a literal translation of the Chinese term cao-yao. It does not necessarily mean that the drugs are only of plant origin. A more appropriate translation would be "folk drugs". Historically, folk drugs evolved from empirical trials and were continuously assimilated into traditional medicine. It is therefore difficult to distinguish the two clearly. However, it is fair to say that the herbal drugs are a more recent concept; they are more often used alone and may be more specific with respect to the treatment.

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*Professor, State Pharmaceutical Administration of China, Beijing

The more important "minority" drugs are from Mongolia and Tibet.

As in occidental medicine, Chinese materia medica comprise materials derived from plants, animal, as well as mineral origin. However, it has been assumed that at least 80 per cent were derived from plants. A recent survey by Xiao ([1], pp. 354-355) has identified 4,877 plant species having some therapeutic value (table 1); the more important plant families are listed in table 2. The contemporary Encyclopaedia of Chinese Materia Medica (Zhong-yao Da Ci-dian) describes a total of 5,767 drugs of plant, animal or mineral origin. Of course, not all of them are recognized. The first volume of the current Chinese Pharmacopoeia (1977 ed.), which devotes itself to Chinese materia medica and their formulations, carries 774 single drug identities including several from minority medicine.

Table 1. Plant species having some therapeutic value

Origin	Number of plant species
Thallophytes	230
Bryophytes	39
Pteridophytes	382
Gymnosperms	55
Angiosperms:	
dicotyledons	3 495
monocotyledons	676
Total	4 877

Source: Xiao Peigen in [1], p. 355.

Table 2. Plant families with over 100 species having some therapeutic value

Plant family	Genera (number)	Species (number)
Compositae	89	331
Leguminosae	91	313
Ranunculaceae	31	208
Labiatae	46	189
Liliaceae	45	165
Rosaceae	28	146
Orchidaceae	45	135
Umbelliferae	34	123
Rubiaceae	35	118
Euphorbiaceae	30	104
Asclepiadaceae	29	101

Source: Xiao Peigen [1], p. 354.

Books on Chinese materia medica

Classical works

It is reasonable to assume that early man, compelled by the need to find food, examined the various substances he encountered and acquired thereby an empirical knowledge of them. Accumulation of this knowledge might have told him that some were palatable and nutritious while others were disagreeable and/or caused adverse effects. This kind of information would have been passed on from generation to generation. The study of nature by man never ceased, and eventually led to the discovery of a group of substances, what today we call drugs, that were notable for their beneficial effect on the sick. Discoveries of drugs were therefore closely connected with studies of edible materials, as evidenced by numerous writings on materia medica throughout history.

In Chinese folklore, the discovery of drugs is accredited to the Emperor Shen-nong, literally the "Divine Peasant". He is said to have tasted a hundred drugs a day and was poisoned by them seventy times. Thus, the first book on Chinese materia medica is named after him - Shen-nong's Herbal (Shen-nong Ben-cao Jing) or The Herbal. The book is believed to have been written between 1 B.C. and 1 A.D. by anonymous authors, and represents a systematic account of all knowledge related to the application of drugs up to that period in Chinese history. Unfortunately, the original text was lost long ago. What is available today is a script re-edited during the Ming and Qing dynasties from quotations contained in many other classics.

Shen-nong Ben-cao Jing as it stands today contains 365 drug items, of which 18 are duplicates. Of the 347 different entities, 239 derive from plants, 65 from animals and 43 from minerals. The book describes pharmacological action and therapeutic value of each drug and classifies them into three categories:

(1) Superior drugs - strengthening and nontoxic; could be administered for prolonged period without harmful effects;

(2) Intermediate drugs - tonic value and effective against diseases; general toxicity dependent on dosage;

(3) Inferior drugs - possessing specific therapeutic activity, but being toxic should not be taken for any prolonged period or in large amounts.

It is amazing to note that most of the drugs described are still in current use. Many, in fact, have been shown by modern technology to possess valuable therapeutic properties, and to have active principles that can be chemically isolated, analysed and synthesized. However, erroneous and detrimental statements involving them do occur, especially in connection with alleged longevity effects.

The Annotations to Shen-nong's Herbal with Records from Famous Physicians (Shen-nong Ben-cao Jing Ji-zhu and Min Yi Bie Lu) came next among the more important classical writings on Chinese materia medica. Written by Tao Hong-jin during Liang (502-536 A.D.) in 7 volumes, the book doubled the listing of drugs to 730 items. It describes the action and use of the drugs and classifies them according to source - jades, stones, herbs, woods, fruits and vegetables, cereals etc.

The Tang Materia Medica/Newly Compiled Materia Medica (Tang Ben-cao/ Xin Xiu Ben-cao) was compiled by 22 scholars including Li Ji and Su Jin in the period 657-659 A.D. under a Royal Decree. It is therefore the first national pharmacopoeia in history.

(It is unfortunate that written transmission of medical texts in China was submerged in utter darkness for hundreds of years - from the end of Han to well into the Sui period (6th-7th century). Textual transmission remained defective until the invention of typography by Bi Sheng far into the Sung period (10th-13th century). Thus, the texts of both the above works are only fragmentary.)

The Classic Classified Materia Medica for Emergencies (Jing Shi Zheng Lei Bei ji Ben-cao) was compiled by Tang Shen-wei towards the end of the 11th century in the Sung period. This became the earliest well-preserved book on materia medica. The book contains 31 volumes plus an extra contents volume and describes the 1,748 drug items.

By far the best known Chinese classic on materia medica is The Compendium of Material Medica (Ben-cao Gang-mu), compiled by Li Shi-zhen in the Ming period, 1552-1578 A.D. However, the book was published only in 1596, after his death. It ran to 52 volumes, described 1,892 drug items with 11,096 related formulations.

Finally came the Supplement to the Compendium of Materia Mexica (Ben-cao Gang-mu Shi Yi). Written by Zhao Xue-min in the Qing dynasty in 1765 A.D., it describes 716 items not listed in the Compendium. This made up a total of 2,608 drugs recorded in formal literature at that time.

The growth in number of recognized drugs over time is illustrated in figure 1. The most important classical writings on Chinese materia medica are summarized in table 3.

Contemporary works

Mainly due to official promotion, several important contributions were published in the three decades since the foundation of the People's Republic.

The Chinese Pharmacopoeia - a major change was made when the pharmacopoeia was issued in two volumes for the first time in 1977. The first volume is devoted entirely to Chinese materia medica, and describes 774 single drugs identities (excluding simple extracts and dosage forms) and 270 compound formulations. Considerable effort has gone into establishing standards for these items. The task, however, is complex.

The Encyclopaedia of Chinese Materia Medica (Zhong-yao Da Ci-dian) was compiled by the Jiang-su College of Novo-medicine and published in Shanghai in 1977 in two volumes with an extra appendix volume. It is the most comprehensive compilation of Chinese materia medica to date - 5,767 drug items are included.

The Chinese Materia Medica (Zhong-yao Zhi), chiefly edited by the Institute of Materia Medica, Chinese Academy of Medical Sciences, was published in Beijing from 1959 onwards in four volumes. This is intended to be an authoritative work describing with meticulous care 494 drug items in detail. The first volume of a second edition, to be completed in six volumes, appeared in 1979.

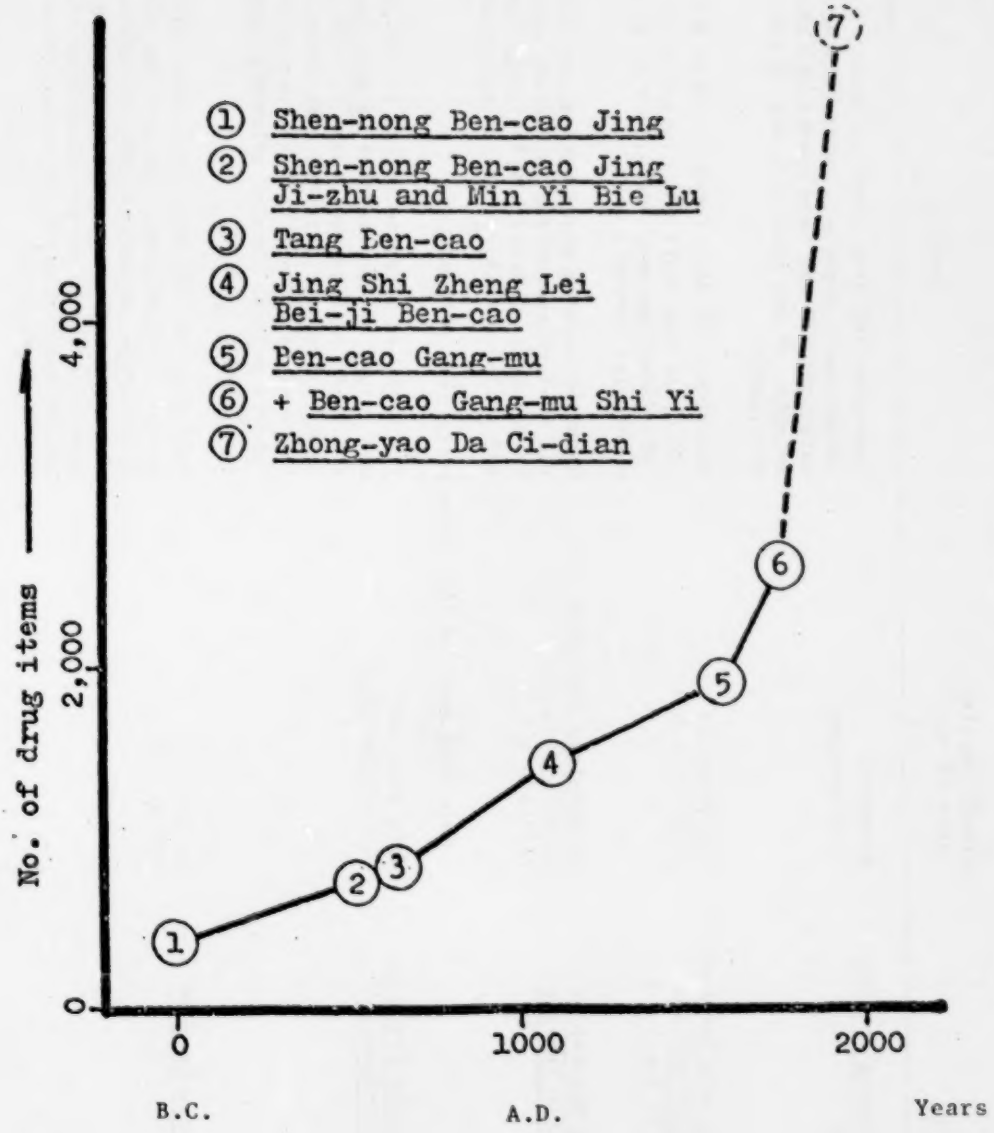

Figure 1. The growth in the number of drug items recorded in classical writings

Table 3. The more important classical writings on chinese materia medica

Title	Author/compiler (date of work)	Content
Shen-nong Ben-cao Jing	Anonymous (1st century)	Describes 365 drug items in three categories - superior, intermediate, inferior; 239 are from plants, 65 from animals, 43 are minerals, and 18 are duplicates
Shen-nong Ben-cao Jing Ji-zhu and Min Yi Bie Lu	Tao Hong-jin (502-536 A.D.)	Describes 730 drug items by their actions and uses; the drugs are classified by source into jades, stones, herbs, woods, fruits and vegetables, cereals etc.
Tang Ben-cao or Xin Xiu Ben-cao	22 scholars including Li Ji and Su Jin (657-659 A.D.)	Compiled under a Royal Decree, the first national pharmacopoeia in history occupies 53 volumes; it describes 844 drugs items, and includes drawings and illustrations
	(Only fragments of the above texts have survived)	
Jing Shi Zheng Lei Bei-ji Ben-cao	Tang Shen-wei (1086-1106 A.D.)	The book was later submitted to the throne and issued by the state as Da-guan Ben-cao; a revised edition was issued in 1116 A.D. as Zhen-he Ben-cao; together they constitute the earliest intact Chinese text of books on materia medica. The 32 volumes describe 1,748 items of drugs
Ben-cao Gang-mu	Li Shi-zhen (1152-1578 A.D.)	Published in 1596 after the death of the author in 52 volumes, the book describes 1,892 drugs, of which 1,094 are derived from plants, 444 from animals and 275 from minerals; the drugs are classified into 16 groups comprising 62 subgroups; there are 11,096 formulations
Ben-cao Gang-mu Shi Yi	Zhao Xue-min (1765 A.D.)	In 10 volumes, the book describes 716 items that are not included in Ben-cao Gang-mu; a further 205 are described in appendices.

Basic concepts in classical medical theory

Early pre-science concepts evolved in China bore a close formal resemblance to those generated in other parts of the world. Though partly lost in transmission, Chinese medical theories have been handed down and further developed through the ages. Admittedly this was sometimes speculative and some fallacies crept in. More significant is the fact that the theoretical aspects of Chinese medicine have always been closely connected with clinical aspects such as observations made during diagnosis and treatment.

Some physiological concepts

The first systematic account of Chinese medical theories appeared in The Inner Classic of the Yellow Sovereign (Huang-di Nei-Jing). It is notable that the material terms used in the classics were not the physical entities, but rather the subdivisions of functional entities. For example, life was considered to be composed of vital essence and spirit, vital energy and blood, humours and fluid (Jing Shen Qi Xue Jing Yie). A biochemical definition was clearly impossible. Another reason for this was that the classical understanding of the body's interior, (Zang-Xiang) is not the equivalent of anatomy. In one recent discussion, the classical view was described as the dynamic interplay of several functional systems, for which the author proposed the term "orbisiconography" [4]. The orbs of five viscera (internal organs) and six bowels in this system are listed in table 4. The former are considered associated with storing life constituents, the latter with digestion and transport of nutrients. Gan, for example, literally corresponds to the liver. The hepatic orb however is a functional entity, and the organ, liver, is merely its substrate or carrier.

The same applies to other orbs. Each is defined not by its anatomic role, but by its specific role in processing, storing and distributing vital energy, and thus in maintaining life.

Table 4. The Orbisiconography

Orb	Anatomical equivalent	Functional entity
Viscera (Yin orbs)		
Xin	heart	cardinal orb
Gan	liver	hepatic orb
Pi	spleen	splenic orb
Fei	lung	pulmonic orb
Shen	kidney	renal orb
(Xin-bao	pericardium	pericardial orb)
Bowels (Yang orbs)		
Dan	gall-bladder	gall-bladder orb
Wei	stomach	stomach orb
Da-chang	large intestine	large intestine orb
Xiao-chang	small intestine	small intestine orb
Pang-huang	urinary bladder	urinary bladder orb
San-jiao	-	triple burners

Another important concept concerns the Jing-luo, often translated as "meridians". This is described in classical Chinese medical theories as a series of conduits or "sinarteries" responsible for distributing energy throughout the body. Many pharmacological actions are ascribed to this functional network of energy flow. Each conduit is conceived as having an orb at one end and a body extremity at the other (see table 5). They are likewise functional rather than anatomical entities.

Table 5. The twelve conduits

The lung conduit of the hand (Tai-yin)
The large intestine conduit of the hand (Yang-ming)
The stomach conduit of the foot (Yang-ming)
The spleen conduit of the foot (Tai-yin)
The heart conduit of the hand (Shao-yin)
The small intestine conduit of the hand (Tai-yang)
The urinary bladder conduit of the foot (Tai-yang)
The pericardium conduit of the hand (Jue-yin)
The triple burners conduit of the hand (Shao-yang)
The kidney conduit of the foot (Shao-yin)
The gallbladder conduit of the foot (Shao-yang)
The liver conduit of the foot (Jue-yin)

Systems of correspondence

The basic ideas common to all Chinese sciences are the polar combination of two opposing principles, Yin and Yang, and the cycle of Wu-xing, i.e. the Five Elements or Five Evolutionary Phases [4] (see figures 2 and 3).

It is from these basic ideas that systems of correspondence are derived. One such system, featuring inductive links between the five elements, the senses, sensory organs and internal organs is shown in table 6.

Classical pharmacology and pharmacological classification of drugs

According to basic concepts of Chinese medicine, the well-being of man depends on maintaining homeostasis. Bodily functions are either Yin or Yang and must work in harmony; the result otherwise is disease. Any deficiency, or excess of heat or cold, either internal or external, is corrected by administering drugs. Thus, cold drugs of a Yin nature are used to treat the heat syndrome of a Yang nature. Conversely, warm-hot drugs of a Yang nature are used to treat the cold syndrome of a Yin nature. Symptoms of deficiency are treated with tonics. Symptoms of excess are treated with purgatives. Ascending symptoms are treated with descending drugs, and descending symptoms with ascending drugs.

It is always the therapeutic effectiveness of a drug that dictates its pharmacological category, and not the reverse. As mentioned earlier, it is unique that the theoretical aspects of Chinese medicine have always retained close links with clinical experience. Chinese medicine is, after all, a practical science. Observations made in diagnosis and during treatment provide a factual basis for reassessing theory.

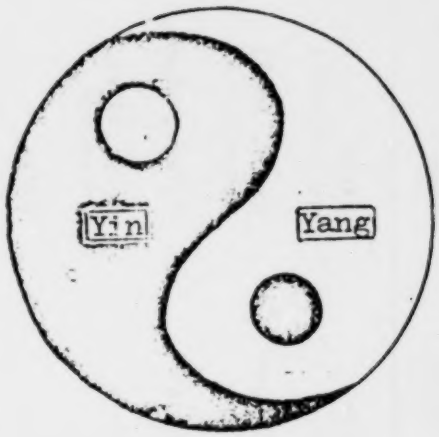

Figure 2. Tai-ji Tu: the balance between two opposing principles, yin and yang

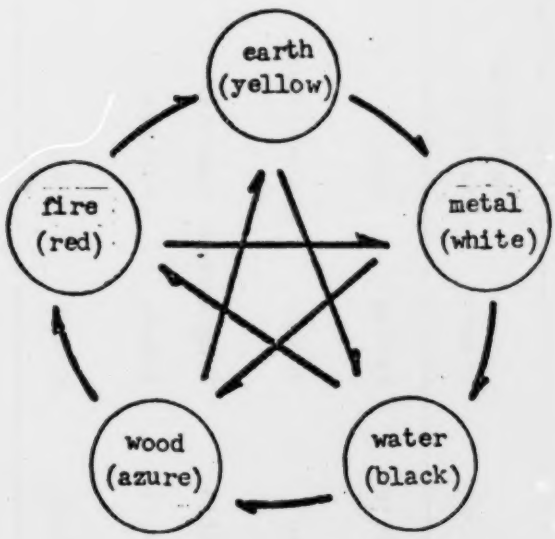

Figure 3. The cycle of five elements

Table 6. A system of correspondence in fives

Elements	Colour	Season	Pathogenic factors	Taste	Sensory organs	Viscera and bowels
Wood	Azure	Spring	Wind	Sour	Eye	Liver, gall bladder
Fire	Red	Summer	Summer-heat	Bitter	Tongue	Heart, small intestine
Earth	Yellow	Long-summer	Dampness	Sweet	Mouth	Spleen, stomach
Metal	White	Autumn	Dryness	Pungent	Nose	Lung, large intestine
Water	Black	Winter	Cold	Salty	Ear	Kidney

Classical pharmacology

Pharmacological characteristics of a drug are described in terms of "four temperaments (properties) and five tastes", "ascending-descending and floating-sinking", "tonic-purgative" etc.

The four temperaments are cold, hot, warm, and cool (Han Re Wen Liang).

Cold and cool are Yin, they differ only in potency. Patients with a heat syndrome such as fever with reddened eyes, thirst and unease or having full and rapid pulse, are advised to administer cold and cool drugs such as Gypsum fibrosum (shi-gao), Rhizoma anemarrhenae (zhi-mu), Rhizoma coptidis (huang-lian), Radix scutellariae (huang-qin) etc.

Conversely, warm and hot are Yang. Patients with a cold syndrome such as pallor, chilliness in extremities, fatigue and sleepiness or having weak pulse are advised to take warm and hot drugs such as Radix aconiti praeparata (fu-zi), Cortex cinnamomi (rou-gui), Rhizoma zingiberis (gan-jiang), Fructus evodiae (wu-zhu-yu) etc. The Yin and Yang distinction is summarized in table 7. There is of course a transition between the two. Drugs bearing temperament in between are said to be moderate (ping).

The five tastes are pungent (acrid), sour, sweet, bitter, and salty. According to Nei-jin "pungent resolves, sour consolidates, sweet moderates, bitter hardens, salty softens". This was the early correlation between tastes and pharmacological effects. Subsequent extensions of these concepts with examples are summarized in table 8.

Every drug has its own temperament and taste, and its pharmacological characteristics depend on both. However, different combinations of temperament and taste give rise to a great variety of drug actions.

Ascending - descending (shen - jiang) are expressions indicating the disposition of drug actions. They are further correlated with the temperament and taste. (Floating - sinking (fu - chen) are similarly correlated, although their relationship seems physical, related to apparent density.)

Here, ascending and floating are Yang. Most drugs of warm and hot temperament, having pungent and sweet taste act in this direction. So are drugs light in weight - flowers, leaves and other voluminous material. On the other hand, descending and sinking are Yin. Most drugs of cold and cool temperament, having bitter, sour or salty taste act in this direction. So are drugs heavy in weight - fruits, seeds and other dense material.

The above correlations are exemplified in table 9. The related pharmacological effects are summarized in table 10.

Pharmacological drug classification

Traditional drugs are classified according to classical pharmacology into the groups and subgroups listed in table 11. With minor alterations, the explanations of the terms in English are those of Xie and Huang [5].

Table 7. Temperaments of drugs and their use in treatment

Temperament	Nature	Drugs cited as examples	Symptoms
Cold and cool	Yin	Gypsum fibrosum (shi-gao) Rhizoma anemarrhenae (zhi-mu) Rhizoma coptidis (huang-lian) Radix scutellariae (huang-qin)	Heat syndrome indicating excessive Yang: fever with reddened eyes, thirst and uneasiness, full and rapid pulse
Warm and hot	Yang	Radix aconiti praeparata (fu-zi) Cortex cinnamomi (rou-gui) Rhizoma zingiberis (gang-jiang) Fructus evodiae (wu-zhu-yu)	Cold syndrome indicating excessive Yin: pallor, chilly extremities, fatigued and sleepiness, weak pulse

Table 8. Correlation between tastes and pharmacological effects

Taste	Viscera acted on	General pharmacology	Example drugs	Therapeutic action
Pungent	Lung	Resolving, invigorating vital energy	Rhizoma zingiberis (shen-jiang) Folia perillae (zi-su)	Resolving, expelling pathogens
			Percarpum citri (reticulate) (chen-pi) Rhizoma cyperi (xiang-fu)	Invigorating vital energy, chest soothing
Sweet	Spleen	Strengthening, moderating	Radix ginseng (ren-shen) Radix astragali (huang-qi)	Strengthening vital energy
			Radix rehmanniae praeparata (shu-di-huang) Radix ophiopogonis (mai-dong)	Nourishing the vital essence (Yin)
			Radix glycyrrhizae (gan-cao) Malt sugar (yi-tang)	Sweetening, moderating and aiding stomach action
Bitter	Heart	Drying dampness purgative	Rhizoma coptidis (huang-lian) Cortex phellodendri (huang-buo)	Drying dampness, expelling internal heat
			Radix et rhizoma rhei (da-huang)	Expelling excessive heat by purging
			Rhizoma atractylodis (cang-zhu)	Drying dampness, improving stomach action
Sour	Liver	Astringent, consolidating	Fructus chebulae (he-zi) Pericarpium granati (shi-lui-pi)	Antidiarrhetic, checking prolapse of anus
			Fructus corni (shan-zhu-yu) Fructus schilzandrae (wu-wei-zi)	Checking spontaneous sweating, arresting seminal emission
Salty	Kidney	Softening hard masses, moistening bowels	Sargassum (hai-zao) Os costaziae (fu-hai-shi)	Resolving phlegm masses and scrofula
			Natrii sulfas (mang xiao)	Moistening bowels, purgative
Non-specific		Promoting excretion and improving resuscitation	Poria (fu-ling) Medulla tetrapanacis (tong-cao) Talcum (hua-shi)	Expelling dampness, diuretic action

Table 9. Correlation between direction of drug action and other pharmacological characteristics

	Ascending and floating drugs	Descending and sinking drugs
Nature	Yang	Yin
Direction of action	Upward	Downward
Temperament	Warm and hot	Cool and cold
Taste	Pungent and sweet, e.g.	Bitter, sour or salty, e.g.
	Herba ephedrae (ma-huang)	Radix et rhizoma rhei (da-huang)
	Ramulus cinnamomi (gui-zhi)	Natrium sulfas (mang-xiao)
	Radix aconiti praeparata (fu-zi)	Radix paeoniae (shou-yao)
	Rhizoma zingiberis (shen-jiang)	Concha ostreae (mu-li)
Weight	Light and voluminous, e.g.	Heavy and dense, e.g.
	Flores magnoliae (xin-yi)	Fructus perillae (zi-su-zi)
	Folia nelumbinis (heye)	Fructus aurantii immaturi (zhi-shi)
	Radix platycodi (jie-geng)	Magnetitum (ci-shi)
	Rhizoma cimicifugae (sheng-ma)	Radix rehmanniae praeparata (shu-di-huang)

Table 10. Pharmacological characteristics and effects of Yin and Yang preparations

Nature	Temperament	Taste	Direction of action
Yang	Warm and hot: Dispelling cold, reinforcing vital	Pungent: Resolving, invigorating vital energy Sweet: Strengthening, moderating Non-specific: Promoting excretion, improving resuscitation	Ascending and floating: invigorating upwards, expelling upwards
Yin	Cool and cold: Dispelling heat, purging internal fire	Bitter: Drying dampness, purgative Sour: Astringent, consolidating Salty: Softening hard masses, moistening bowels	Descending and sinking: checking exuberance of vital function, supressing upward flow; consolidating, promoting excretion, expelling heat, purging

Table 11. The pharmacological classification of drugs

Drugs for dispelling pathogens from the exterior of the body, i.e. diaphoretics (jie-biao yao):
- (a) With pungent taste and warm temperament (xin wen jie-biao yao)
- (b) With pungent taste and cool temperament (xin liang jie-biao yao)

Antitussives (anticoughing), anti-asthmatics, and drugs for resolving phlegm:
- (a) Warm drugs for resolving cold phlegm (wen hua han-tang yao)
- (b) Cool drugs for resolving heat phlegm (qin hua re-tan yao)
- (c) Antitussives (zhi-ke yao)
- (d) Anti-asthmatics (pin-chuan yao)

Drugs for clearing internal heat, i.e. antipyretics (qin-re yao):
- (a) Drugs for clearing up and purging intense internal heat (qin-re xie-huo yao)
- (b) Drugs for clearing up heat and cooling the blood (qin-re liang-xie yao)
- (c) Drugs for clearing up heat and dampness (qin-re zao-shi yao)
- (d) Drugs for clearing up heat and pathogens (qin-re jie-du yao)

Drugs for dispelling internal wind and dampness, i.e. antirheumatics (qie-fong-shi yao)

Warm drugs for dispelling internal cold (wen-han yao)

Aromatic drugs for resolving dampness (fang-xiang hua shi yao)

Diuretics and hydrogogues (li-niao shu-shui yao):
- (a) Diuretics and mild hydrogogues (li-niao sen-shi yao)
- (b) Hydrogogues or drastic purgatives (zhu-shui yao)

Drugs for regulating the flow of vital energy (li-qi yao)

Drugs for regulating blood condition and circulation (li-xie yao):
- (a) Haemostatics (zhi-xie yao)
- (b) Drugs invigorating blood circulation and resolving blood clots (huo-xie hua-yu yao)

Aromatic drugs for stimulating resuscitating (fang-xiang kai-qiao yao)

Drugs stabilizing the spirit (an-shen yao) - essentially sedatives and tranquilizers

Drugs for subduing hyperactivity of the hepatic orb and endogenous wind (pin-gan xi-fong yao)

Drugs reinforcing vital functions, i.e. tonics and aphrodisiacs (bu-yang yao):
- (a) Drugs for replenishing vital energy (bu-qi yao)
- (b) Drugs for nourishing the blood (bu-xie yao)
- (c) Drugs for replenshing vital essence (bu-yin yao)
- (d) Drugs for reinforcing the vital function (bu-yang yao)

Drugs arresting discharges (gu-se yao) - including astringents and haemostatics

Digestives and evacuants (xiao-dao yao)

Purgatives and laxatives (xie-xia yao)

Anthelmintics (gu-chong yao)

Drugs for external use (wai-yong yao)

Compounding of drugs

According to the guidelines for formulation, a prescription comprises four different ingredients:

(a) The principal (jun, the king) ingredient - provides the principal curative action;

(b) The adjuvant (chen, the minister) - helps strengthen the principal action;

(c) The auxiliary (zuo, the assistant) ingredient - relieves secondary symptoms or tempers and action of the principal ingredient when the latter is too potent;

(d) The conductor (shi, the usher) - either directs the action to the affected conduit or site, or acts as a less significant auxiliary ingredient.

Of course, the delineation in some cases may not be clear; also more than one ingredient may be involved in one component part.

Seven modes of drug interaction

Experience shows that drugs may interact when dispensed together. The modes of interaction are as follows:

(a) Acting alone (dan-xin) - application of a strong single action, such as ginseng in a simple ginseng decoction;

(b) Mutual reinforcement (xiang-xu) - action between two ingredients with similar properties, e.g. the reinforcing effect between Rhizoma anemarrhenae (zhi-mu) and Cortex phellodendri (huang-bo) in nourishing vital essence and suppressing pathogenic heat;

(c) Assistance (xiang-shi) - action of one or more ingredients with dissimilar properties to strengthen another principal drug, e.g. Radix astragali (huang-qi) as a vital energy replenisher used to strengthen the diuretic action of Poria (fu-ling);

(d) Counteraction (xiang-wei) - interaction between ingredients so that one reduces the potency or toxicity of the other. Thus Rhizoma zingiberis (shen-jiang) is used in processing Rhizoma pinelliae (ban-xia) in order to eliminate the latter's toxicity.

(e) Mutual restraint (xiang-wu) - interaction between ingredients so that one restrains the activity of the other. For example, when used together, Radix scutellariae (huang-qin) can weaken the warm temperament of Rhizoma zingiberis (shen-jiang);

(f) Neutralization (xiang-sha) - interaction between ingredients so that one counteracts toxic reactions produced by another. For example, Radix ledebouriellae (fang-feng) can neutralize the toxicity of arsenic oxide (pi-shuang);

(g) Incompatibility (xiang-fan) - indicates that when used together two ingredients will result in severe side effects or toxicity, e.g. Radix glycyrrhizae (gan-cao) and Radix euphorbiae kansui (gan-sui).

Eight therapeutic methods

In Chinese traditional medicine drugs are compounded for eight different therapeutic purposes: diaphoresis, emesis, purging, mediation, invigoration, heat reduction, stimulation and resolution (han, tu, xia, he, wen, qin, bu, xiao).

The pharmacological classification of drugs is also closely associated with these therapeutic methods.

Comparison with Western materia medica and the concepts of classical pharmacology

As even a cursory study shows, there are many points of similarity between east and west in the historical development of material medica, especially in the concepts of classical pharmacology.

Babylonian-Assyrian and Egyptian materia medica

Over 300 drugs are mentioned in Babylonian-Assyrian tablets. In some instances, the drugs are listed in special groups, for example, drugs for heart ailments. On the other hand, most of our knowledge of ancient Egyptian therapeutics is obtained from the Ebers Papyrus which was discovered by George M. Ebers in 1872. The Papyrus dates from 1550 B.C. and describes more than 700 drugs.

Graeco-Roman materia medica

Early Greeks such as Pythagoras (580-489 B.C.) took lessons from Egyptians and Pythagoras himself went on to make important contributions on the theoretical side (see next section). Like the early Chinese, another famous Greek, Hippocrates (460-377 B.C.) believed in a dietary regime. Thus, substances such as barley meal and ptisan (barley extract), honey preparations, mustard, pepper etc. were included in Greek materia medica.

The most important pharmacological treatise of the Graeco-Roman period was the authoritative text of Dioscorides (1st century), written at about the same time as the Shen-nong's Herbal. It is arranged alphabetically and was used as a pharmacological handbook for approximately 1,600 years. Many of the drugs included are still in use today, e.g. acacia, aconite, aloe, bitter almond, elaterium, cantharides, gentian, liquorice, poppy etc.

Concepts in classical pharmacology

Because later European medicine was largely developed on the basis of Graeco-Roman tradition, concepts in classical pharmacology formed during Graeco-Roman period continued to exert an influence until the dawning of modern medical science in the middle of the 19th century. It is in this connection that we find the best analogy between East and the West.

Four elements, four qualities, and humours

The theories of four elements, four qualities and four humours evolved throughout the Graeco-Roman period - from Pythagoras (580-489 B.C.) through Empedocles (490-430 B.C.) to Galen (130-200 A.D.). The theory of four elements (figure 4) states, that all matter is composed of fire, air, water and earth, and that they are interchangeable by means of compression or rarefaction. The qualities of the elements are said to be manifest as heat, dryness, cold and moisture respectively. Heat and cold are said to be active contraries, dryness and moisture are passive contraries. (Compare Yin and Yang and the five elements.)

It was probably Hippocrates (460-377 B.C.) who advanced the concept of humour. This considers that food after ingestion undergoes a process of extraction from which it emerges in a semifluid state and is then taken up by the body. By Galen's time, this biological theory had become rigidly formulated and was merged with the apparently physical theory of four elements, taking the final shape shown in the lower part of figure 4.

Bodily constituents

Life itself was considered by the Greeks to depend on pneuma which was breathed in from the air. The pneuma made its way into the blood and was then responsible for the phenomenon of neural conduction. As shown in figure 4, the Greeks considered the black bile, yellow bile, the blood and phlegm as essential bodily constituents. (Compare Qi and Xie.)

Pharmacology

Galen maintained that "it is the business of pharmacology to combine drugs in such a manner - according to their elementary qualities of heat, cold, moisture, and dryness - as shall render them effective in combating or overcoming the conditions which exist in the disease" [3].

Four temperaments and seven tastes

Paul of Aegina (625-690 A.D.) was a Byzantine researcher and the author of a large medical text in seven volumes. The last of the books is very voluminous and is devoted to materia medica. The first two sections express lucidly the ideas of the period - the so-called four temperaments (drying, moistening, cooling, or heating) and the associated seven tastes. These bear a remarkable similarity to the Chinese classification shown in table 8:

(a) Astringent - contracting, obstructing, condensing, dispelling, and incrassating (swelling); cold and desiccative;

(b) Acid - cutting, dividing, attenuating, removing obstructions and cleansing without heating; cold;

(c) Acrid - resembles the acid in being attenuating and purging, but differs from it in being hot;

(d) Bitter - cleansing the pores, detergent and attenuating, cuts thick humours without sensible heat; watery and therefore cold;

(e) Salty - contracting, bracing, preserving, drying; neither hot nor cold;

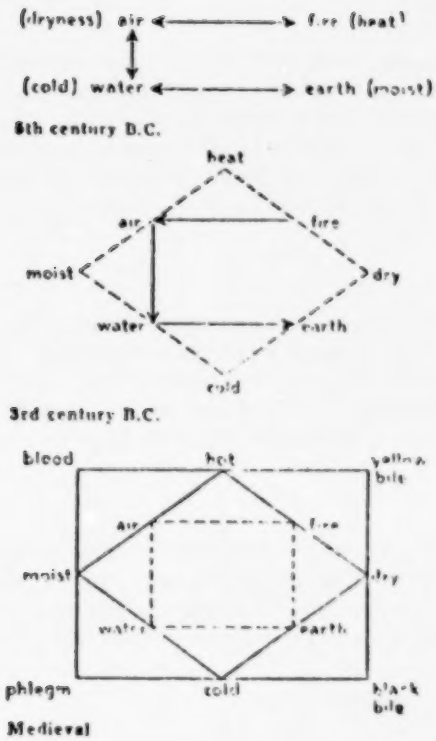

Figure 4

Source: C.C. Mettler [3].

(f) Sweet - relaxing, concocting, softening, and rarefying;

(g) Oily - humectating (moistening), softening, and relaxing.

Arabic contribution - Avicenna's medical canon

The Canon is essentially a summary of Graeco-Arabic medicine. Its materia medica covers 760 drugs. From the 12th to 17th centuries this work served as the chief guide to medical science in the West and is still in occasional use in the Moslem east.

The concept of the organism as a whole

Treating the whole organism is one of the most important principles in Chinese traditional medicine. Quite similar statements can also be found in Graeco-Roman medical literature. For example, Alconaeon (6th century B.C.) says that health is the balance and disease the maladjustment of such forces as heat, cold, dryness, moisture; for Hippocrates, treatment of a disease is the removal of deteriorated humours of the body by means of sweating, diarrhoea, and emesis - similar in other words to the Chinese therapeutic methods.

Further prospects

The modern age of materia medica

After the Renaissance, the progress of European medicine was very slow. Not until the middle of the 19th century did achievements in the basic sciences pave the way for medical advancement. The advent of a new era in medicine was initially signalled by the introduction of general anaesthesia (ether, 1842; nitrous oxide, 1844; chloroform, 1847) and phenolic antiseptics (1867). The contributions from the following then formed the foundation for the construction of an entirely new medicine - modern medicine:

Claude Bernarde	(1813-1878)
Rudolf Virchow	(1821-1902)
Louise Pasteur	(1822-1895)
Robert Koch	(1843-1910)
Paul Ehrlich	(1854-1915)

The construction of a new medicine would have been impossible, however, without the parallel advancement of new materia medica. In particular, the work of Paul Ehrlich, initiated towards the end of the 19th century, pointed the way. The search for new drugs since then has been carried out in a controlled way in the laboratory. Drug research, in other words, became a science.

Shortcomings

Ehrlich's idea was to find a specific "bullet", a "magic bullet" that could destroy pathogenic organisms without affecting the host. The development of antibiotics, especially the β-lactams that attack the cell wall structure of the bacteria, approximates to this. However, experience showed that Ehrlich's original idea seemed to have oversimplified the situation, even in the field of chemotherapy. This is even more the case when research work is carried out on functional diseases. There are serious methodological problems associated, for example, with the programming of screening tests. This is, of course, one of the factors that has made the development of new drugs increasingly costly.

What can be expected of Chinese materia medica?

Chinese materia medica are for the most part easily accessible to people living in rural areas. The so-called "bare-foot doctors", being peasants themselves can cultivate, collect, process, and utilize medicinal plants for the benefit of their communities. Home-made herbal preparations play a significant role in primary health care and help lessen the burden of medical expenses.

There is a great wealth of clinical experience accumulated in the application of Chinese materia medica to the treatment of various diseases. If these diseases were identified in modern terminology, then drugs active in treatment could be subjected to appropriate screening programmes in order to isolate their active principles. Further modification of their chemical structure might lead to more effective compounds.

However, classical drugs are seldom used alone in Chinese traditional medicine. They usually go into formulations according to the kind of rules described earlier. Analytical studies of formulations with respect to a defined scope of treatment may lead to simplified recipes, or even to identifying the active drug and thus to the isolation of active compounds. For example, according to the Chinese Pharmacopoeia (1977 ed.) the classical Su-hc xiang-wan (a compound containing styrax) is composed of 15 drug components. However, by pharmacological screening, the formulation was first reduced to five then finally to only two components, styrax and borneolum.

Many of the principles of classical treatment have proved invaluable, or at least complementary to modern therapy. They might contain truths that have not yet een uncovered by Western science. Elucidation of the action mechanism of th drugs concerned may point the way to further developments in new drug research.

From the above, it can be seen that there are ample opportunities for development and exploitation.

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BASIC CONCEPTS OF CHINESE TRADITIONAL MEDICINE

By Xie Zhufan*

A B S T R A C T

Chinese traditional medicine was formed under the guidance of ancient Chinese philosophy - the theory of Yin-Yang and the Five Evolutionary Phases - and has undergone a long process of improvement and enrichment over a period of more than two thousand years.

The human body is viewed as an organic whole with a close relation to the external environment. The fundamental mechanism of disease is conceived as a breakdown of the equilibrium within the organism or between the organism and the external environment, either due to deficiency of life constituents and resistance capacity or due to the harmful effects of pathogenic factors.

The life constituents and resistance capacity of the body include the dynamic energy for physiological activities (Qi) the heat energy for metabolism (both of which pertain to Yang), and the essential substances such as vital essence, blood and body fluids (which pertain to Yin).

The common pathogenic factors are "atmospheric" (wind, cold, heat damp, dryness and fire), pestilential pathogens, trauma, emotional factors, improper diet, overstrain etc.

In clinical diagnosis the need to differentiate the syndromes that reflect the pathogenesis and pathophysiology of the morbid condition is emphasized, including its cause, nature and location, as well as the confrontation between the resistance capacity and the pathogenic factors.

Syndromes can be classified into two or three main categories: those showing insufficient body resistance, diminished functional activities or deficiency in essential substances (deficiency syndromes); those showing overabundance or excess of pathogenic factors (excess syndromes); and combined syndromes of deficiency and excess.

The general treatment principle for deficiency syndromes is to strengthen the patient's resistance capacity, to promote the physiological activities and to replenish the required substances; with excess syndromes the approach is to remove or dispel the pathogenic factors.

Deficiency syndromes can be further divided into deficiencies of Yin, Yang, Qi and blood each of which has its specific therapeutic method with corresponding herbal drugs, e.g. to nourish or replenish Yin when Yin is in deficiency. (The drugs used for this pupose are called Yin-replenishing tonics.)

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*Associate Professor, Beijing Medical College, Beijing.

Excess syndromes can be further classified according to the relevant pathogenic factors, such as wind syndrome, cold syndrome, heat syndrome etc. Each excess syndrome also has its specific therapeutic method and corresponding drugs. The diagnosis of syndrome, method of treatment and selection of drugs should always work in conjunction with each other.

Since the treatment is directed against the syndrome rather than the disease, different diseases may be treated by the same method if they are alike in pathogenesis and clinical manifestations; conversely different methods of treatment may be applied to the same kind of disease in the light of different physical reactions.

Because of their different historical backgrounds, Chinese traditional medicine and Western medicine show striking differences - not only in their practical experience, but also in their theoretical aspects. Chinese medical theories were formed on the basis of accumulated practical experience under guidance of an ancient philosophy of dialectics. Such philosophical reflections can be found in every medical field, but they are particularly important in the concept of health and disease, and the principles of diagnosis and treatment.

Health and disease

The human body is regarded both as a whole organism whose various parts are closely related to each other, and as an organic unit adapted to the natural environment. Health implies that co-ordination between various parts of the human body, the human body's adaptation to variations in the natural environment, and the balance between functional activities and the supply of essential substances are kept in a normal range. Once there is discordance, non-conformity or imbalance, illness occurs. Thus, the fundamental mechanism of disease is the breakdown of a relative equilibrium within the organism or between the organism and its environment. Consequently, medical treatment should be aimed at restoring the normal equilibrium.

The onset and development of a disease is taken as the result of a confrontation between the resisting capacity of the human body and the harmful effect of pathogenic factors. It is this confrontation that breaks the normal equilibrium. Both pathogenic factors (see below) and body resistance may play important roles in pathogenesis and sometimes the latter is even more emphasized than the former. For example, The Classic of Internal Medicine (Nei Jin) points out: "When there is abundant body resistance, invasion by pathogenic factors is impossible ... a pathogenic factor such as wind, rain, cold or heat itself is unable to damage the human body unless there is insufficient body resistance. Some people with good resistance, though caught in a heavy rain and strong wind, do not become ill. Therefore, merely the pathogenic factor itself is not enough to cause a disease." Emphasis on the internal cause in aetiology is in fact one of the characteristic features of Chinese traditional medicine. It has had a great influence not only on the concept of disease, but particularly upon the principles of treatment.

Pathogenic factors

The limitation of natural sciences and technology meant that traditional medicine was unable to use instruments and research equipment to discover pathogens -- as modern medicine does. Pathogenic factors were discovered chiefly by observation and analysis of their clinical manifestations. This made traditional aetiology unique. Although not entirely logical from a modern perspective, it is still useful in clinical practice because it is closely related to therapeutic effects.

In Chinese traditional medicine, pathogenic factors can be classified into the following categories:

(1) Atmospheric factors. There are six kinds of atmospheric changes commonly experienced: wind, cold, summer-heat, damp, dryness and fire. Most of these changes are related to seasons, and in ordinary conditions they do no harm to human beings. But if they go too far (for example becoming too hot or too cold) or occur at the wrong time (such as being warm in winter or cool in summer), they may become pathogenic because the human body does not adapt to them. Diseases caused by atmospheric factors are therefore usually related to seasons.

There is no clear-cut boundary line between the normal and abnormal (non-pathogenic and pathogenic) atmospheric changes. It is therefore not always possible to ascertain the atmospheric change as the cause of disease merely from the weather or climate itself. In fact, the terms wind, cold, heat, damp, dryness and fire are used more frequently to designate different patterns of clinical manifestations, suggesting the invasion of these factors rather than to designate the weather changes. Thus, diseases caused by atmospheric factors are by no means limited to those related to excessive changes of weather. In fact seasonal infectious diseases are also attributed to the attack of atmospheric factors.

(2) Emotional factors. Emotions such as joy, anger, melancholy, anxiety, grief, fear and fright may lead to disease if they are in excess (i.e. if they are very intense and persistent or the individual is hypersensitive to stimulation). Here, the emotions rather than the stimulation from the environment is considered the pathogenic factor. For this reason diseases caused by emotional factors are called endogenous injuries, while those caused by atmospheric factors are exogenous infections.

(3) Other pathogenic factors. Improper diet, irregular food intake, over-strain or stress, trauma etc. may also be harmful to health and cause disease.

Body resistance

The resisting capacity of the body includes all the vital energy, essential substances and physiological activities needed to maintain normal life processes and protect the body against pathogenic factors. In traditional medical terminology they are Yin, Yang, Qi (energy) and Xue (blood).

Yin denotes the structural or material aspect of the organism, especially the essential substances such as vital essence and fluids. Blood, of course, is also included in Yin, but it is often considered separately in order to stress its importance. Yang denotes the functional aspect of the organism, especially the heat energy required to maintain normal metabolism, and the dynamic energy required to accomplish various physiological activities including the defensive energy needed to ward off the attack of exogenous pathogens. Qi usually refers to the dynamic energy mentioned above, so it pertains to Yang. Since dynamic energy is invisible and its existence can only be recognized by observing the functional activities produced by it, Qi is often used as a synonym for functional activity, and deficiency of Qi of a certain organ usually implies hypofunction of that organ.

Differentiation of syndromes

The Chinese traditional medicine differentiation of syndromes (concurrent symptoms) is often more important for making decisions on therapeutic regimes than diagnosing the actual disease. Though the concept of disease also exists in traditional medicine, most such diseases are actually referred to by their main symptoms or external signs - such as headache, asthma, oedema (swelling), jaundice etc. Thus, diagnosis of disease alone in its traditional sense is obviously inadequate as a guide to treatment.

Differentiation of syndromes is based on an overall analysis of symptoms and signs, including the cause, nature and location of the illness as well as the nature of the confrontation between the pathogenic factors and body resistance. In Chinese medicine, a syndrome is not a simple summation of symptoms and signs: in each case it should reflect the pathogenesis and pathophysiology of the morbid condition.

Classification of syndromes

There are several different classifications of syndromes, of which the most practical is one primarily based upon the nature of the confrontation between the pathogenic factors and body resistance. In this classification, all syndromes can be classified into two or three main categories: (1) syndromes showing insufficient body resistance, diminished functional activities or deficiency in essential substances (deficiency syndromes); (2) syndromes showing overabundance or excess of pathogenic factors (excess syndromes); and (3) combined syndromes of deficiency and excess.

Deficiency syndromes can be divided into the following groups:

(1) Deficiency of Yin. According to the theory of Yin-Yang, Yin and Yang are two opposites of a single entity; decrease or deficiency of the one usually leads to relative increase or excess of the other. Thus, deficiency of Yin is often associated with production of endogenous heat (pertaining to Yang), marked by low or hectic fever, feverishness in the palms and soles, emaciation, night sweating, thirst, condensed urine, constipation, reddened and furless tongue, thready and rapid pulse.

(2) Deficiency of blood. This results from profuse haemorrhaging, chronic loss of blood or impaired blood production, usually manifested by pallor, dizziness, palpitation, insomnia, menstrual disorders etc.

(3) Deficiency of Qi. General manifestations are weakness, lassitude, listlessness, shortness of breath, feeble pulse etc. Deficiency of Qi of a given organ is usually manifested by hypofunction of that organ.

(4) Deficiency of Yang. Since the Yang of the human body comprises the dynamic energy for physiological activities (Qi) and the heat energy for metabolism ("Vital Fire"), deficiency of Yang can be defined as deficiency of both Qi and heat energy, or hypofunction of visceral organs with manifestations of "cold" such as intolerance of cold, cold extremities etc.

The above deficiency syndromes may be general or only involve one or two visceral organs. In the latter case the visceral organs involved should be mentioned in the syndrome diagnosis, e.g. deficiency of Qi of the lung (marked by decreased respiratory function), deficiency of Yin of the lung (marked by dry cough or expectoration of scanty sputum with blood streaks).

Excess syndromes are usually classified according to the overabundant pathogenic factors. The common excess syndromes are as follows:

(1) Wind syndromes (including the syndromes that are caused by attacks of the wind or bear some similarity to symptoms or signs of natural wind phenomena).

Physical wind is air in motion: it rises and falls in short periods and is usually stronger at the top of a hill than at the bottom. Thus symptoms with the following characteristic features are believed to be caused by the wind and are grouped into the exogenous wind syndromes: (a) symptoms or morbid conditions with sudden onset and quick disappearance in a short period, e.g. acute urticaria; (b) morbid conditions with lesions constantly moving from one place to another, e.g. rheumatic arthritis with migratory joint pain; (c) morbid conditions with symptoms more marked at the top of the body, e.g. acute nephritis with oedema in the face; (d) aversion to physical wind, which suggests attack of the body surface by the wind, e.g. common cold. (In Chinese traditional medicine a mild common cold is usually referred to as "catching wind" or "affection by the wind".)

Some of the syndromes can indeed be caused or precipitated by exposure to wind, but others have only a resemblance to the natural phenomena caused by the wind in certain respects. Obviously it is not logical to draw conclusions of causation merely on the basis of similarity. Nevertheless, all of them can be successfully treated with "wind-dispelling" drugs.

There is another group of symptoms characterized by sudden onset of abnormal involuntary movements or by sensation of abnormal movements - such as tremor, twitching, convulsion, vertigo, fainting, and apoplexy. They also belong to wind syndromes since they have some aspects resembling the natural phenomena of wind. In fact, they have nothing to do with natural wind and are treated in an entirely different way from syndromes caused by exposure to wind. To distinguish them, they are called syndromes of endogenous or internal wind, and are considered produced by dysfunction of internal organs.

(2) Cold syndromes. Exogenous cold syndromes refer to infections by exogenous cold, such as common colds with marked chilliness, arthritis with pain aggravated by exposure to cold, and abdominal pain and diarrhoea after catching cold.

Cold syndromes may also be caused by lowered production of heat energy in the body-marked by intolerance of cold and cold limbs. They are manifestations of deficiency of Yang and hence pertain to deficiency syndromes.

(3) Heat syndromes. Heat causes feverishness, thirst, fidgets and sweating. It accelerates blood circulation and dilation of blood vessels, bringing about a flushed face, reddened tongue and rapid pulse. Diseases with the above symptoms are attributed to heat. Most cases of febrile disease have heat syndromes. Heat syndromes due to exogenous pathogenic factors are of the excess type; those due to deficiency of Yin are of the deficiency type.

(4) Damp syndromes. Damp makes things sticky and diseases caused by damp are thus often lingering. Damp makes things heavy, and the patient with damp syndrome often feels heaviness in the head, body or limbs. Damp can turn to turbid liquid, and thus turbid discharges such as leucorrhoea, turbid urine and exudation from skin lesions are still attributed to damp. Damp may impede the normal flow of vital energy in the body, and thus produce sensations of fullness in the chest. Dyspnoea and coughing with profuse expectoration may occur when the lung is impaired. Epigastric or abdominal distension, anorexia, nausea and diarrhoea accompanied by thick greasy coating of the tongue may occur when the digestive system is affected.

Damp may be exogenous, due to a wet environment, or endogenous, due to disordered fluid metabolism in the body. In either case the damp is taken as a pathogenic factor and should be expelled from the body in the treatment.

(5) Dryness syndromes. Since the respiratory system is in direct contact with a dry atmosphere, exogenous dryness is usually marked by dry mouth, dry lips, dry nose, dry throat and dry cough. Syndromes of dryness can also be caused by deficiency of body fluid after profuse vomiting, diarrhoea, perspiration or haemorrhaging, or due to high fever or chronic consumption. All these states of fluid deficiency lead to endogenous dryness syndromes which are of the deficiency type.

(6) Fire syndromes. Fire is characterized by intense heat and red flames. Thus acute inflammations with local redness and heat or fever are usually attributed to fire. The pathogenic fire or intense heat is apt to impair the body fluid, leading to thirst and desire for cold drinks, constipation and oliguria. It may also injure the blood vessels causing bleeding. Infection by exogenous pathogenic factors may cause fire syndromes, but dysfunction of visceral organs due to emotional factors may also give rise to them.

(7) Phlegm syndromes. The concept of phlegm in Chinese traditional medicine is much broader than that in Western medicine. It refers to all the mucous substances either spat or vomited, or retained in the body. Although phlegm is a kind of pathological product, it may serve as a pathogenic factor and lead to further pathological changes if not eliminated in time. It is believed that phlegm may be formed if fluid is accumulated in a certain part of the body and condensed. Phlegm affecting the respiratory system causes coughing, asthma and expectoration of sputum. In addition, apoplexy, epilepsy, hysteria and mania are also attributed to phlegm, which, unlike the phlegm in the respiratory tract, never comes out of the body and hence is invisible. Subcutaneous nodules such as enlarged lymph nodes are also taken as local retention of phlegm.

(8) Syndromes of Qi stagnation. Various phatogenic factors can impede the normal flow of Qi (vital energy) causing its stagnation, with pain and distension as the main symptoms. Since a stagnant Qi is harmful to health and should be dispelled, syndromes with Qi stagnation are of the excess type - though their primary cause may be a deficiency condition.

(9) Syndromes of blood stasis. Stagnant blood, in retarded circulation, coagulation or extravasation, may lead to further pathological changes. The common symptoms and signs caused by blood stasis are severe local pain (often accompanied by tenderness), mass formation, ecchymoses or petechiae, purple tongue or purple spots on the tongue. Coronary heart disease, diseases involving enlarged liver and spleen, dysmenorrhoea, ectopic pregnancy, traumatic injuries etc. usually show syndromes of blood stasis.

Principles of treatment

Treatment in Chinese traditional medicine is chiefly based upon the differentiation of syndromes. In cases of deficiency syndromes the general principle of treatment is to strengthen the patient's resistance, promote physiological activity and replenish the required substances. In excess syndromes the treatment should be chiefly aimed at removing or dispelling the pathogenic factors.

Classification of treatment conforms with the classification of syndromes. For deficiency of Yin replenishment of Yin (vital essence and body fluid) with corresponding tonics is indicated; for deficiency of blood, toning up the blood; for deficiency of Qi, reinforcement of vital energy; for deficiency of Yang, invigoration of vital functions with drugs warm or hot in nature. The drugs used for deficiency syndromes are called tonics, and they fall into at least four categories: Yin-replenishing tonics, blood tonics, Qi-replenishing tonics and Yang-invigorating tonics.

For excess syndromes, the therapeutic methods are more varied. Different methods should be used for dispelling different pathogenic factors; sometimes different methods should be applied even for the same pathogenic factor, when it is located in different parts of the body.

Wind syndromes. For exogenous wind syndromes, administration of drugs to dispel the pathogenic wind are prescribed. Most of the wind-dispelling drugs are diaphoretics and antirheumatics. However, these drugs are not prescribed for treating endogenous wind, which can only be subdued by sedatives and anticonvulsives.

Cold syndromes. When the attack of cold is limited to the surface of the body, the treatment aims at dispelling the pathogenic cold from the body exterior with pungent and warming sudorifics. But if the interior portion of the body is invaded by cold, drugs for dispelling internal cold are indicated. These drugs can also be used when the cold syndrome is produced by deficiency of Yang.

Heat syndromes. When the attack of heat is limited to the surface of the body, the treatment aims at dispelling the pathogenic heat with mild cooling diaphoretics, pungent in flavour. When there is pathogenic heat in the body interior, the general principle is to clear up the internal heat. Different drugs should be used to remove pathogenic heat from different visceral organs or areas of the body.

Damp syndromes. The general treatment principle is to dispel the pathogenic damp. Different methods should be applied depending on the patient's condition. In mild cases, drugs to resolve damp are recommended. In severe cases, elimination of the pathogenic damp by drying is preferable. For damp syndromes marked by oedema, diuresis is indicated.

Dryness syndromes. The general treatment principal is moistening. Drugs to dispel the pathogenic factors are only indicated in cases of exogenous dryness. Most cases of dryness are due to deficiency of body fluid and should be treated with drugs for replenishing Yin (fluid).

Fire syndromes. The general principle is to quench the pathogenic fire. As when treating internal heat, different drugs should be used for removing pathogenic fire from different visceral organs or areas of the body. Since fire syndromes can also be caused by emotional factors leading to hyperactivity of certain visceral organs, quenching the fire in some cases implies reducing the hyperactive functioning of those organs.

Phlegm syndromes. The general principle is to dispel phlegm. The drugs used for phlegm syndromes of the respiratory system include expectorants, antitussives and anti-asthmatics. However, since apoplexy, epilepsy, hysteria, mania, and even tuberculosis of the lymph nodes are attributed or partially attributed to phlegm, some drugs to dispel phlegm can also be used for those diseases.

Stagnation of Qi. Its treatment is to regulate the flow of Qi (vital energy). Most of the drugs used for this purpose are pungent flavoured carminatives.

Blood stasis. The principle is to promote blood circulation and to eliminate blood stasis. The drugs for both are in the same category, but different in strength of action. The former are milder while the latter more drastic. Some also have analgesic effect.

As shown above, the classification of herbal drugs groups them according to their actions and their relationship to syndromes. The diagnosis of syndrome, principle of treatment and selection of drugs should always work in concert.

Since the treatment is directed against the syndrome instead of the disease, different diseases may be treated by the same method if they are alike in clinical manifestations and pathogenesis; similarly, different methods of treatment may be applied to the same kind of disease in the light of different physical reactions and clinical manifestations.

Although a single drug can be given for the treatment, in most cases compound prescriptions of several ingredients are used. Various ingredients are combined in a prescription for the purpose of producing a desired therapeutic effect in unison and reducing toxic or side effects. Generally speaking, the ingredients can be classified into four groups: the principal, adjuvant, auxiliary and conductor. The principal ingredient provides the principal curative action; the adjuvant helps strengthen the principal action, the auxiliary relieves secondary symptoms or reduces side effects of the principal ingredient; the conductor directs action to the affected site. A compound prescription may thus have advantages over a single drug.

CLINICAL APPLICATIONS OF TRADITIONAL AND HERBAL DRUGS

By Li Shun Cheng*

A B S T R A C T

The use of medicinal herbs in China dates back to antiquity. Rich experience has been accumulated in the use of traditional Chinese medicinal herbs in clinical practice. Most show good effects against common diseases and have been proved by modern research to posess extensive pharmacological properties.

The article introduces the clinical use of Chinese medicinal herbs classifying them into four categories on the basis of the kinds of diseases to which they are applied.

(a) Infectious diseases: according to traditional Chinese medicine, infectious diseases usually belong to syndromes of heat, noxious-dampness or damp-heat. Clinically, febrifugal and detoxicant drugs or drugs for clearing up the pathogenic damp-heat (Flos lonicerae, Fructus forsythiae, Herba taraxaci, Radix isatidis) are used. These drugs act as antipathogenic organisms, showing antipyretic activity and anti-inflammatory action. Some regulate the body's immunological function. In order to improve the blood circulation and promote absorption of anti-inflammatory drugs for eliminating pathogenic heat from blood and for removing blood stasis (Radix paeoniae rubra, Cortex moutan radicis) have to be included. For weak patients, especially those with chronic infectious diseases, tonics (Radix ginseng, Radix astragali) should be selected.

For example, in treating boils, carbuncles and cellulitis, Flos lonicerae, Fructus forsythiae, Herba taraxaci are often preferred. Radix isatidis and Herba taraxaci are very effective in treating infections of the upper respiratory tract associated with high fever, sore throats and actue tonsillitis.

(b) Cardiovascular diseases: according to traditional Chinese medicine, hypertension is a syndrome of the disorder of Yin and Yang, i.e. Yin being insufficient and Yang being in excess. Drugs for nourishing Yin (Radix rehmanniae, Ramulus loranthi, Concha ostreae usta) and those for reducing Yang (Rhizoma gastrodiae, Ramulus uncariae cum uncis) should be used in combination. Since coronary heart disease is mainly related to blood stasis, drugs for promoting blood circulation and removing blood stasis should be applied. Tonics for improving the general bodily functions and those of the heart may be used if necessary.

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*Associate Professor, Department of Combined Traditional Chinese and Western Medicine, Beijing Medical College, Beijing.

(c) Common diseases of the digestive system: since acute gastritis and enteritis pertain to the damp-heat syndrome in the stomach and intestine, drugs for removing heat and eliminating dampness (Radix scutellariae, Rhizoma coptidis) are often used. Acute infectious hepatitis also results from infection by damp-heat and should be treated with drugs to clear up damp-heat

in the liver along with other herbs to relieve jaundice or improve the liver function (Radix tsatidis, Radix bupleuri, Fructus schisandrae). Chronic gastritis and peptic ulcer show a syndrome of weakness in the spleen and stomach and should be treated with tonics (Radix astragali, Radix condonopsis Pilosulae); antacid herbal drugs or spasmolytics may be added if necessary.

(d) Parasitic diseases: herbal treatment of ascariasis, enterobiasis and taeniasis, and the antimalarial drug - Qinghaosu - are recommended. The latter is effective for treating malignant and tertiary malarias. It kills the malaria parasite and has a quick action.

For reference to clinical practice, some common herbal drugs and recipes are given for each of the diseases mentioned above.

China's use of medicinal herbs and traditional therapeutic principles to treat common diseases mostly involves compound prescriptions rather than single drugs. The following discussion considers the herbal therapy for common infections, cardiovascular diseases, digestive disorders and parasitic diseases.

Common infectious diseases

Infectious diseases include a large number of diseases manifested by acute inflammation of the body surface or internal organs. These are due to either local invasion of bacteria or viruses or invasion through the blood stream.

Infectious diseases are usually classified clinically according to the infected location, i.e. surgical infections, such as boils, carbuncles, cellulitis, lymphodenitis and systematic or organic infections (such as infections of the respiratory, digestive or urinary system, ears, nose, throat and eyes). In serious cases, general infection (such as toxaemia or septicaemia) may result.

The occurrence and development of infectious disease is not only due to the pathogenisis of bacteria and viruses, but also linked with lowering of body resistance.

Although there are many kinds of acute infectious diseases, their causes and pathological changes are nearly the same; their treatments are also similar. According to modern medicine, the chief aim is to eliminate the effect of pathogens.

According to the theory of traditional Chinese medicine, in contrast, most of the acute infectious diseases show the syndromes of heat, noxious-damp and damp-heat. This calls for a combination of febrifugal and detoxicant drugs together with drugs to clear up the pathogenic heat and dampness.

The following treatments are used for common acute infectious diseases.

Boils, carbuncles and cellulitis

These diseases commonly occur among labourers. Large doses of antifebriles and antitoxicants should be used. Other general therapy may be necessary for treating carbuncles and cellulitis.

Possible drugs:

Flores lonicerae, Fructus forsythiae, Herba taraxaci, Herba violae, Flores chrysanthemi idici, Herba andrographitis, Rhizoma bistortae etc.

Prescription examples:

(a) Generally two to three kinds of the above drugs, 15-30 g each, according to the degree of infection. The drugs should be taken in the form of a decoction (extracted essence);

(b) A double decoction of: Flores lonicerae, 30 g; Flores chrysanthemi indici 20 g; Radix glycyrrhizae 6 g;

(c) A decoction of: Herba taraxaci, 30 g; Herba violae, 15 g; Radix paeoniae rubra, 12 g; Flores chrysanthemi indici, 15 g.

Acute tonsillitis

Chiefly caused by infection of haemolytic streptococcus, acute tonsillitis is characterized by a quick attack, often accompanied by high fever (body temperature may reach 39 to 40°C), sore throat, tonsils distinctly reddened and swollen, covered with purulent exudation. The treatment principle is use of drugs with antifebrile and antitoxic effects.

Possible drugs:

Herba taraxaci, Radix isatidis, Flores lonicerae, Fructus forsythiae and Radix sophorae subprostratae.

Prescription examples:

(a) A compound decoction of: Radix isatidis, 30 g; Radix sophorae subprostratae, 6 g; Radix glycyrrhizae, 6 g;

(b) Liu-shen pill - 5 to 10 pills to be melted in mouth and then swallowed.

In one test 88 hospitalized patients suffering from acute tonsillitis, 55 with body temperatures ranging from 37.5°C to 39.0°C, 33 with temperatures over 39°C, all suffering from sore throat and inflammation and purulent exudation of the tonsils, were given tablets made of Herba taraxaci alone. The dose was 15 tablets four times a day, each tablet containing 0.5 g Herba

taraxaci. Of the group, 95 per cent (82 cases) were cured in one to three days. Pharmacological investigations have also shown that Herba taraxaci has a broad antimicrobial spectrum and is capable of promoting the body's own immunological activity.

Infection of the upper respiratory tract

Upper respiratory tract infections are caused by bacteria or viruses and are generally called common colds. They are characterized by local inflammatory changes accompanied by the following clinical manifestations: chilliness, fever, stuffy nose with nasal discharge, or dry and sore throat.

According to traditional medical theory the above symptoms pertain to the "exterior" syndrome and should be treated with diaphoretics or drugs expelling the pathogens from the body exterior. If there is marked fever and severe pain in the throat, administration of febrifugal and detoxicant drugs are also necessary.

Possible drugs:

For patients with chills and nasal watery discharge but showing no sore throat, diaphoretics with a warm characteristic should be used - such as Herba ephedrae, Rhizoma zingiberis, Folia perillae, Herba schizonepetae. If the patient has fever, dry and sore throat, febrifugal and detoxicant drugs should be used in larger doses, and diaphoretics with cold characteristic should be added - such as Flores lonicerae, Fructus forsythiae, Radix isatidis, Herba menthae.

Prescription examples:

(a) A decoction of: Radix isatidis 30 g;

(b) A decoction of: Rhizoma dryopteridis 15 g; Folia isatidis, 15 g.

Influenza, of course, is a very common infectious disease of the upper respiratory tract. Its onset is very rapid with symptoms more serious than that of a common cold. It is therefore necessary to take active measures to prevent it spreading, in addition to the method of treatment. For treatment, Radix isatidis, Flores lonicerae, or Fructus forsythiae should be prescribed in large doses. For prevention, smaller doses of the drugs mentioned above or Rhizoma dryoptridis or Folium isatidis may be used.

Extract of Radix isatidis made in medicinal granules is now widely used in China to prevent and cure influenza. Modern pharmacological studies have demonstrated its antiviral action on influenza and mumps viruses. Moreover, it has a broad-spectrum bacteriostatic action, and also increases the phagocytosis of the reticulo-endothelial cells and leucocytes.

As mentioned above, febrifugal and detoxicant drugs are very effective in treating acute infectious diseases. Their pharmacological action can be summarized as follows:

Antipathogenesis
Strengthening of the defensive mechanism of the body
Regulating the immunological state of the body

Antipyretic action
Detoxicant action
Anti inflammatory action.

Common cardiovascular diseases

In China the most common diseases of the circulatory system are hypertension, coronary heart disease and acute occlusive cerebrovascular disease. In recent years some experience has been obtained in treating them with herbal drugs, especially those that promote blood circulation and eliminate blood stasis.

Hypertension

Hypertension may be classified into primary and secondary types. Secondary hypertension is caused by other diseases, such as renal, endocrinal or intracranial lesions. For these it is therefore necessary to treat the original lesions. Primary hypertension is a general chronic disease, the cause of which is still not clear. Most investigators believe that it is related to strong mental strain or irritation over a prolonged period. This causes functional disorder of the nervous and endocrinal system and induces spasm and sclerosis of arterioles, resulting in elevation of blood pressure.

According to traditional Chinese medicine, this disease is a manifestation of the disorder of Yin and Yang, i.e. Yin is insufficient and Yang is too abundant. Experiments showed that most drugs for nourishing Yin are capable of regulating the function of the nervous and endocrinal system. Drugs for subduing Yang have sedative and hypotensive activities. In order to improve the cardiovascular functions, prevent or reduce arteriosclerosis, drugs for promoting blood circulation and eliminating blood stasis should be used in combination.

Possible drugs:

(a) Tonics to regulate the nervous and endocrinal systems - Radix rehmanniae, Radix polygoni multiflori, Fructus lycii, Ramulus loranthi;

(b) Drugs to reduce Yang or having a hypotensive effect - Rhizoma gastrodiae, Radix scutellariae, Flores chrysanthemi indici, Spica prunellae, Ramulus uncariae cum uncis, Folia apocyni veneti;

(c) Drugs to promote blood circulation and eliminate blood stasis; drugs for dilating blood vessels, improving the heart function and preventing or reducing arteriosclerosis - Radix paeoniae rubra, Rhizoma ligustici chuanxiong, Fructus crataegi, Herba leonuri, Radix puerariae.

Prescription examples:

(a) A daily decoction of: Flores chrysanthemi indici, 15 g; Spica prunellae, 10 g; Ramulus loranthi, 20 g;

(b) A decoction of: Folia apocyni veneti, 10 g, Flores chrysanthemi indici, 10 g;

(c) A decoction of: Rhizoma gastrodiae, 10g; Ramulus uncariae cum uncis, 10 g; Spica prunellae, 10 g.

Experimental investigation has shown that Rhizoma gastrodiae and Ramulus uncariae cum uncis have a distinct hypotensive effect toward renal hypertensive animals, and at the same time improve the nervous function. Ramulus uncariae cum uncis also act to dilate blood vessels and strengthen the activity of acetylcholine. Radix puerariae has shown good effects in relieving cerebral vasospasm and improving cerebral blood circulation.

Coronary heart disease

Coronary heart disease is caused by sclerosis of the coronary arteries. The patient feels a paroxysmal precordial pain spreading to the left shoulder and arm. During myocardial infarction, an electrocardiogram often shows characteristic changes. It is therefore necessary to improve the function of coronary arteries in order to increase coronary blood flow so that the anoxic (oxygen deficient) impairment of myocardial function may be relieved.

According to traditional Chinese medicine, this disease is mainly related to blood stasis. Drugs to promote blood circulation and eliminate blood stasis should therefore be used. Tonics for improving general and heart functions should be added whenever necessary.

Possible drugs

(a) Drugs to promote blood circulation and eliminate blood stasis - these drugs improve the function of the heart, dilate the coronary arteries and remove or prevent formation of arteriosclerosis and thrombosis - Radix notoginseng, Radix salviae miltiorrhizae, Rhizoma ligustici chuanxiong, Radix paeoniae rubra, Radix puerariae, Flores carthami, Herba leonuri, Radix angelicae sinensis.

(b) Tonics to improve general and heart functions - Radix ginseng, Radix codonopsis, Rhizoma polygonati odorati, Radix polygoni multiflor.

Prescription examples:

(a) A daily double decoction of: Radix salviae miltiorrhizae, 30 g; Radix notoginseng, 6 g;

(b) A daily double decoction of: Radix salviae miltiorrhizae, 15 g; Flores carthami, 10 g; Rhizoma ligustici chuanxiong, 15 g; Radix paeoniae rubra, 15 g.

Common diseases of the digestive system

Diseases of the digestive system may be classified into acute and chronic types. Acute gastritis, enteritis, dyspepsia and hepatitis are the most common acute digestive diseases. Chronic gastritis, enteritis, peptic ulcer and chronic hepatitis are the most common chronic digestive diseases. Experience has shown that good results may be obtained using herbal medicines.

Acute gastritis and gastro-enteritis

Chief symptoms are quick attacks of vomiting and stomach-ache. The above symptoms accompanied by abdominal pain and watery diarrhoea is acute gastro-enteritis.

Because the disease attacks quickly and the patient vomits sour and bitter fluid and can suffer from fever, it belongs to the syndrome of damp-heat in the stomach and intestine. As noted earlier the fundamental manifestation of the damp-heat syndrome is pathological inflammation with distinct discharge.

Treatment principles:

(a) Remove heat and eliminate dampness with febrifugals and diuretics; this relieves the inflammatory reaction of the gastro-intestinal tract;

(b) Promote diuresis and inhibit diarrhea;

(c) Adopt combined therapy - traditional Chinese and western medicine - if serious dehydration or continuous vomiting and diarrhoea occur.

Possible drugs:

(a) Febrifugal, dampness-dispelling and detoxicant agents: most of these drugs inhibit intestinal bacterial flora and relieve intestinal inflammation - Radix scutellariae, Rhizoma coptidis, Herba taraxaci, Radix puerariae, Herba agostachis, Herba eupatorii;

(b) Diuretics: use diuresis to stop diarrhoea and relieve intestinal oedema - Poria, Semen plantaginis, Rhizoma alismatis.

Prescription examples:

A double decoction of: Radix puerariae, 15 g; Radix scutellariae, 10 g; Rhizoma coptidis 3 g; Radix glycyrrhizae 6 g.

Modern pharmacological studies have shown that the above prescription produces distinct antipyretic, antibacterial and anti-inflammatory action.

Acute infectious hepatitis

Acute infectious hepatitis is caused by the invasion of hepatitis virus. Chief symptoms are poor appetite, general debility, nausea, vomiting, aversion to cold and fever. If accompanied by dark yellow urine and yellowish sclera, it is called acute icteric hepatitis; if the symptoms are not so serious, i.e. the GPT level (glutamic pyruvic transaminase) in liver-function examination shows some elevation, but there is no jaundice, it is called anicteric hepatitis.

According to traditional Chinese medicine, acute infectious hepatitis falls in the category of affliction by heat and damp. Hence it should be treated with drugs clearing up heat and damp together with herbs relieving jaundice or improving the function of the liver. Pharmacological studies have shown that these drugs produce antiviral and chologogic actions while improving the liver-function and reducing GPT levels.

Possible drugs:

(a) Drugs capable of eliminating damp-heat in the liver and bile tract - Radix isatidis, Radix bupleuri, Radix scutellariae, Radix glycyrrhizae, Herba sedi sarmentosi, Herba patriniae, Fructus schizandrae, Ganoderma lucidum. Experiments have shown that Radix isatidis and Radix scutellariae produce antiviral activity and are effective for hepatitis; Fructus schizandrae, Ganoderma lucidum, Radix glycyrrhizae are capable of promoting the synthesis of liver glycogen and protein, and ameliorating liver damage; Fructus schizandrae is effective in reducing GPT level; Radix eupleuri in combination with Radix clycyrrhizae is able to improve liver metabolism and protect the liver from damage;

(b) Cholagogues - drugs that increase the secretion and excretion of bile, that protect the liver from damage and show a distinct effect in reducing jaundice - Herba artemisiae scopariae, Fructus gardeniae, Radix curcumae, Rhizoma curcumae longae, Radix bupleuri, Radix aucklandiae, Herba taraxaci.

Prescription examples:

(a) A double decoction for acute icteric hepatitis: Radix isatidis, 20 g; Herba artemisiae scopariae, 30 g; Rhizoma imperatae, 30 g;

(b) A double decoction for anicteric hepatitis: Herba artemisiae scopariae, 30 g; Radix bupleuri, 10 g; Fructus schizandrae, 10 g; Radix glycyrrhizae, 6 g.

Chronic hepatitis may be treated with the above drugs in combination with tonics such as Radix astragali, Radix angelicae and Ganoderma lucidum.

Peptic ulcer

Peptic ulcers include gastric and duodenal ulcers. Their cause is not yet fully understood, but they may be due to the functional disorder of the central nervous system, hyperchlorhydria, that lowers the resistance of gastroduodenal mucous membrane so that it is susceptible to attack by gastric acid.

A special feature of this disease is prolonged, chronic, intermittent attacks of upper abdominal pain, the timing of which closely relates to intake of meals. It is often accompanied by regurgitation of acid, heartburn sensation and belching.

According to traditional Chinese medicine, this disease shows a syndrome of weakness in the spleen and stomach, and should be treated by regulating the function of the intestine and the stomach, thus producing antacid activity, spasmolysis, analgesia and promoting the healing of the ulcer.

Possible drugs:

(a) Drugs to invigorate the spleen and regulate the vital energy. These drugs have the effect of regulating the function of the nervous system, especially that of the vegetative nervous system. They also improve the

functions of the gastro-intestinal tract, reduce gastric secretion, protect the gastric mucous membrane from damage and promote healing of the ulcer - Radix astragali; Radix codonopsis pilosulae, Radix glycyrrhizae;

(b) Antacid herbal drugs - Ossa sepiae, Herba taraxaci;

(c) Spasmolytics: Bulbus fritillariae thunbergii, Rhizoma corydalis, Radix paeoniae alba, Radix glycyrrhizae.

Experiments have shown that Bulbus fritillariae thunbergii has an atropine-like effect; Radix glycyrrhizae has a spasmolytic and analgesic effect, and is able to reduce secretion of gastric acid, thereby promoting healing of the ulcer; Rhizoma corydalis has a distinctive spasmolytic and analgesic effect.

Prescription examples:

(a) Ossa sepiae, 30 g; Rhizoma bletillae, 30 g; Radix glycyrrhizae, 20 g; to be powdered and mixed, 1 to 2 g to be taken orally, three times a day;

(b) Radix astragali, 15 g; Ramulus cinnamomi, 10 g; Radix paeoniae alba, 30 g; Radix glycyrrhizae, 6 g; taken as a double decoction.

Common Parasitic Diseases

Ascariasis (roundworm disease)

Prescription examples:

Fructus quisqualis, 5 g. Before use, the pericarp should be removed and the seed baked and stirred to a yellowish colour. It is chewed and swallowed once a day at bedtime, and may be taken for two to three successive days.

Cortex Meliae, 15 g; to be taken as a double decoction before meals, once a day for two successive days.

Enterobiasis (pinworm disease)

Pinworm disease may be treated as described above for ascariasis.

Taeniasis (tapeworm disease)

Prescription examples:

(a) Semen arecae: taken as a 35 per cent decoction (100-300 ml) in the morning before a meal. If necessary, 15-20 g magnesium sulphate may also be taken;

(b) Semen cucurbitae, 30 to 60 g to be swallowed after chewing, in the morning before a meal.

Combined use of (a) and (b): (a) is administered first; (b) is given after two hours.

Agrimophol is isolated from a Chinese medicinal plant, Agrimonia pilosa and made up into tablets, (tab. agrimopholi 0.1 g). Eight tablets are taken in the morning before a meal. Magnesium sulphate, 20-30 g, is given after four hours. For children, the dose is 25 mg per kg body weight.

Malaria

Qinghaosu (artemisinine) the active ingredient isolated from a Chinese medicinal plant, Artemisia annua, is effective for treating malignant and tertiary malaria. It kills the malaria parasite without side-effects, acts quickly, and is also effective for chloroquine-resistant cases. Qinghaosu is divided into three doses of 0.3 to 0.4 g to be taken each day, for three successive days.

As the above brief introduction on the use of herbal drugs to treat certain common diseases shows, medicinal herbs and their preparations have good prospects. They are not only therapeutically effective, with few harmful side-effects, but also easily obtainable from our own country's natural resources. Their use therefore conforms with the principle of promoting the people's health on the basis of self-reliance.

MODERN RESEARCH ON CHINESE TRADITIONAL AND HERBAL DRUGS

By Xiao Peigen*

A B S T R A C T

Chinese traditional drugs, which have been used by the Chinese people over a long period of history, still play an important role today in China's health service.

In this paper, a brief review of research on Chinese traditional drugs includes investigation and systematization, resource utilization and examples of approaches to searching for new drugs. In addition some of the new drugs originating from Chinese traditional drugs are tabulated by pharmacological activity, e.g. those affecting the cardiovascular system, the nervous system and/or the respiratory system; those with potential for family planning; and those having anti-cancer, anti-microbial, parasiticidal and/or immunostimulatory action.

Some 60 new drugs have evolved directly or indirectly from Chinese herbal medicine by means of interdisciplinary scientific methods. As a result many are now available commercially, for example the total isoflavones of Pueraria lobata, tetramethylpyrazine from Ligusticum chuanxiong, anisodamine (-)6β-hydroxyhyoscyamine) from Scopolia tangutica. This shows that traditional drugs are an important source for new drugs and industrial production.

Introduction

Chinese traditional drugs, which have been used by the Chinese people over a long period, still play an important role in the people's health service of today.

To date 1,152 items of crude drugs, which are mainly Chinese traditional drugs along with their preparations, have been recorded in the latest edition (1977) of the Chinese Pharmacopoeia [1]. Furthermore, Chinese traditional drugs are estimated to account for 30-50 per cent of total medicament consumption, i.e. they are comparable with synthetic drugs and antibiotics in China.

This is mainly due to Government promotion and development of Chinese traditional medicine. One of the more important measures in this context is the use of modern multidisciplinary methods to raise the traditional medicine to a more scientific level.

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*Professor, Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing.

Investigation and systematization

Modern research aims primarily at an understanding of Chinese traditional drugs that includes their origin, distribution, resources, and therapeutic usage.

A nation-wide survey has found more than 5,000 items of crude drugs are now in use in China. Based on this many books have been published, of which the three most important are:

(1) The Chinese Materia Medica, compiled by the Institute of Materia Medica and others. The old edition contained 994 items of drugs in 4 volumes; the new edition will be in 6 volumes, the first of which appeared in 1979 and the second in 1981.

(2) The Atlas of Commonly Used Chinese Traditional Drugs (1970), was also compiled by The Institute of Materia Medica and others. This booklet includes 240 drug items, each of them illustrated by a colour painting. It serves as a tool for popularizing the knowledge of Chinese traditional drugs - including identification, evaluation, collection, processing and application.

(3) The Dictionary of Chinese Traditional Drugs (1977), compiled by Nanjing College of Traditional Chinese Medicine, comprehensively describes 5,767 Chinese traditional drugs.

Resource utilization

In order to make use of the drug resources considerable attention has been paid to the theory of correlating the phylogeny, chemical constituents and pharmaceutical aspects of plants.

This work was first used in the search for domestic resources for the imported drugs (see table 1). It was then extended to explore new resources of some important Chinese traditional drugs, for instance, Salvia multiorrhiza, Schizandra chinensis and others. This was the origin of a new tropane alkaloid-containing drug - Przewalskia tangutica - with hyoscyamine and total alkaloids content amounting to 1.67-3.82 per cent and 2.06-4.01 per cent, respectively [2].

Table 1. Examples of domestic resources for the imported drugs

Imported drug	Domestic resource
Rauwolfia serpentina	R. verticillata, R. yuanensis, R. latifrons
Styrax benzoin	S. hypoglauca, S. tonkinensis
Strychnos nux-vomica	S. wallichiana
Acacia senegal	A. farnesiana, A. decurrens
Picrorhiza kurroa	P. scrophuriae (flora)
Hydnocarpus anthelmintica	H. hainanensis
Ferula asafoetida	F. sinkiangensis

A third use of this correlation is in drug evaluation. This has given good results with drugs such as Chinese rhubarb, mudapi and shaoyao etc.

Approaches to finding new drugs

Research guided by experiences of Chinese traditional medicine

In recent years, following systematic investigation of the Chinese traditional antimalarial drug Artemisia annua, it has been found that the neutral fraction of its ether extract showed marked malariacidal effects in Plasmodium berghei in mice and P. inui and P. cynomolgi in monkeys. Toxicological studies showed no obvious side-effects in animals and a clinical study on 30 patients also gave satisfactory results. Further laboratory investigation led to the isolation of an active component Qing Hao Su. Clinical studies of different Qing Hao Su preparations were carried out in 2,099 cases of malaria. All patients were clinically cured.

Exploring ancient literature on Chinese traditional medicine

In the course of treating hypertension among factory workers, it was found that blood pressure could be reduced to normal or to a suitable level. However, many of the patients still suffered from headache, dizziness and a stiffness and soreness in the neck. In the ancient classic Shang Han Lun, it is recorded Ge Gen Tang, (a decoction that has the root of Pueraria lobata as its chief ingredient) is recommended for treating stiffness and soreness in the neck. Following this therapeutic lead, a series of clinical trials of a preparation of Pueraria lobata gave satisfactory results. Chinese phytochemists then isolated and identified the active components as the isoflavones daidzein, daidzin, puerarin, and daidzein-4', 7-diglucoside. Pharamacological studies revealed that either the total isoflavone or the single compound puerarin was capable of increasing the cerebral and coronary blood flow, decreasing the oxygen consumption of the myocardium and increasing the blood oxygen-deficient heart muscle. These actions could partially explain the mechanism of the Pueraria preparations used for the relief of hypertensive disease, angina pectoris, migraine and sudden deafness. Daidzein has shown a papaverine-type spasmolytic action, and its clinical trials demonstrated an action similar to the total isoflavone preparation. Total synthesis of daidzein has now been accomplished and is currently being developed for industrial production.

Exploring "secret" prescriptions

In 1970, a secret prescription for antitaenia used by a 79-year old peasant in northeast China was investigated. The method of treatment had involved an oral dose of 50 g of the powdered winter bud of Agrimonia pilosa (Gemma Agrimoniae) taken on an empty stomach. Five to six hours after administering the drug, not only the segments, but also the scolex of the worm could be eliminated. Sixty-eight patients were treated in a hospital by a similar regimen with an effectiveness as high as 98.5 per cent. The active principle of Gemma agrimoniae was then isolated, and its structure elucidated and named agrimorphol. This compound was submitted to clinical study and its efficacy fully substantiated. It is now in use as a commercial product.

Using the treatment principles of Chinese traditional medicine

In Chinese traditional medical treatment is conducted under the guidance of systematic principles, the three most common of which are summarized in table 2 together with their possible correlation with the western diagnoses.

An example is an investigation of the blood circulation stimulant drug Ligusticum chuanxiong (L. wallichii) (rhizome) Chuan Xiaong from which more than ten compounds were isolated. Among these tetramethylpyrazine was found to be the active principle, but it was present only in minute amounts in the plant. Pharmacological and clinical studies revealed that tetramethylpyrazine hydrochloride could improve microcirculation in the mesenteroids of rabbits, and could also dilate capillary vessels, in vitro. Tetramethylpyrazine not only inhibited platelet aggregation caused by adenosine diphosphate (ADP), but also disaggregated the aggregated platelets. Clinically, it can be used with satisfactory results for treating occlussive cerebral blood vessel diseases, such as cerebral embolism. It is now being manufactured on a large scale synthetically.

Table 2. The three most common treatment principles of Chinese traditional medicine, their possible correlation with western diagnoses and examples of drugs used

Treatment principles	Relation to western diagnosis	Examples of drugs used
Mobilization of blood circulation and treatment of stasis (Huo Xue Hua Yu)	Cardio-vascular diseases, thromboangiitis, obliterans, cerebral embolism	Ligusticum chuanxiong (rhizome), Carthamus tinctorius (flower), Typha latifolia (pollen), Crataegus pinnatifida (fruit), Angelica sinensis (root), Paeonia lactiflora (root), Salvia miltiorrhiza (root)
Promotion of vigour and stabilization of vitality (Fu Zheng Gu Ben)	As general tonic, for treating weakness; probably with an immuno-stimulating action	Astragalus membranaceus var. mongholicus (root), Panax ginseng (root), Codonopsis pilosula (root), Acanthopanax senticosus (root)
Treatment of fever, and inflammation; detoxication (Qing Re Jie Du)	Antibacterial, antiviral anticancer; possibly with an immuno-stimulating action	Coptis chinensis (rhizome), Indigo naturalis, Scutellaria baicalensis (root)

Using leads from the phenomena of drugs acting on the human body

Schisandra chinensis (fruit) (Wu Wei Zi), a Chinese traditional drug commonly used as an astringent, was found clinically to exhibit therapeutic effects on certain forms of hepatitis, particularly in lowering the elevated serum glutamic pyruvic transaminase (SGPT) level. This immediately aroused the interest of physicians as well as pharmacists. In detailed chemical and pharmacological studies, it was found that the active principles responsible for lowering elevated SGPT levels were a series of derivatives belonging to the dibenzo [a,c] cyclo-octene series. Among the derivatives, Schizandrer B, Schizandrol B and Schizandrin C showed the best protective activity against liver damage induced by CCl_4.[4/] The ethanol extract of the kernel of this drug is now used for this purpose.

Clinical results from applications of traditional drugs used by national minorities

Scopolia tangutica (root) (Tangchom Nagbo), is a drug used in traditional Tibetan medicine in Qinghai, a western inland province. Overdosages of this medicine caused symptoms of atropine toxicity.

Phytochemical investigation revealed that besides hyoscyamine and scopolamine, it contained anisodamine and anisodine. Pharmacological studies indicated that the effect on the central nervous system of anisodamine is 6 to 25 times weaker than that of atropine, and the effect of anisodine on the peripheral nervous system is weaker than both atropine and scopolamine. Clinically, anisodamine has been used to treat septic shock from toxic bacillary dysentery, fulminant epidemic meningitis and haemorrhagic enteritis. Anisodine is now used to treat migraine and diseases of the fundus occuli caused by vascular spasm, organophosphorus poisoning, and acute paralysis caused by cerebral vascular accidents; it is also used as the chief component in Chinese traditional anaesthesia.

Anisodiamine and anisodine are now being produced commercially.

As the result of a study of phylogenetic relationships among Chinese solanaceous plants, a notable new tropane alkaloid-containing plant, Przewalskia tangutica (root and plant) (Tangchom gaabo), was found. This plant is also a commonly used Tibetan traditional drug. Its high total alkaloids and hyoscyamine contents were noted above.

Other results

Since 1949 there have been over 1,000 scientific reports in this field. Many new drugs originated from the Chinese herb medicine are listed and grouped under different pharmacological actions in table 3 [1, 3-7].

Table 3. New drugs originating from Chinese traditional drugs

Drug	Active principles[a/]
Drugs with anti-cancer activity:	
Rabdonia rubescens (plant)	Oridonine, ponicidine
Polyporus umbellatus (plant)	Zhu-ling polysaccharides
Crotalaria sessiliflora (plant)	Monocrotaline, alkaloid II
Iris pallasii var. chinensis (seed)	Irisquinone
Atractylodes macrocephala (rhizome)	Volatile oil, atractylon, butenolide B
Sophora alopecuroides (root)	Sophocarpine
Curcuma aromatica (rhizome)	Volatile oil, curcumol, curdione
Mylabris phalerata	Cantharidin and its synthetic
M. cichorii (whole)	Derivative N-hydroxycanthridinimide
Drugs affecting cardiovascular system:	
Salvia miltiorrhiza (root)	Phenanthrene-quinone; tanshinone II-A; water soluble fraction
Angelica sinensis (root)	Volatile oil; ferulic acid
Uncaria rhynchophylla (stem)	Total alkaloids and rhynchophylline
Buxus microphylla var. sinica	Cyclovirobuxine D
Ilex pubescens (root or leaf)	Total extract, flavonoids and scopoletin, Aesculetin
Drugs affecting the nervous system:	
Corydalis turschaninovii f. yanhusuo (rhizome)	dl-Tetrahydropalmatine
Sinomenium acutum (stem)	Sinomenine
Gastrodia elata (rhizome)	Gastrodin
Datura metel (flower)	Scopolamine
Loranthus parasiticus parasited on Coriaria sinica (plant)	Tutin
Patrinia scabiosaefolia (root)	Volatile oil, patrinene, isopatrinene and saponin
Drugs for family planning:	
Gossypium hirsutum (seed, root)	Gossypol
Trichosanthes kirilowii (root)	Protein of Trichosanthes
Daphne genkwa (root)	Yuanhuacine A and B

continued

Drug	Active principles[a/]
Drugs acting on liver:	
Sedum sarmentosum (plant)	Sarmentosine
Artemisia scoparia (young plant)	Chlorogenic acid, caffeic acid, hydroxyacetophenonum 6,7-dimethoxy-coumarin
Swertia mileensis (plant)	Oleanolic acid
Armilariella tabescens (mycelium)	Armillarisan A
Drugs affecting respiratory system:	
Rhododendron dauricum (leaf)	Farrerol, germacrone, scopoletin
Vitex negundo var. *cannabifolia* (leaf)	Volatile oil, β-caryophyllene
Roripa indica (plant)	Rorifon
Cymbopogon distans (plant)	Piperitone
Ardisia japonica (plant)	Bergenin
Drugs with antimicrobial effects:	
Houttuynia cordata (plant)	Volatile oil, decanoyl acetaldehyde
Fagopyrum cymosum (rhizome)	5,7,3',4'-tetrahydroxyflavane-3-nol C_4-C_8 dimer
Pyrola rotundifolia (plant)	Methylhydroquinone (methylquinol)
Ardisia japonica (plant)	Ardisinol I and II
Lysionotus pauciflorus (plant)	Nevadensin
Salvia miltiorrhiza (root)	Total tanshinone, cryptotanshinone
Drugs for treating parasite infection:	
Melia toosendan (root, bark)	Chuanliansu
Cucurbita moschata (seed)	Cucurbitin
Artabotrys hexapetalus (root)	Qingzhaosu A
Drugs with immuno-stimulating action:	
Astragalus membranaceus var. *mongholicus* (root)	Astragalin (polysaccharide)
Acanthopanax senticosus (root)	Polysaccharide
Allium sativum (bulb)	Diallyl thiosulfonate

a/ For structures of selected active principles, see appendix.

Other research on Chinese traditional drugs has also been carried out. This includes improvement of processing techniques, research on the classical theory of traditional medicine, and cultivation and tissue culture of some of the more important traditional drugs.

Discussion

The viewpoints expressed here place more stress on multidisciplinary scientific research than on the features of Chinese traditional medicine. The examples illustrate the relationships that, by linking together the traditional experiences of Chinese herb medicine and modern scientific research, result in new drug discoveries. These relationships are outlined as in the figure.

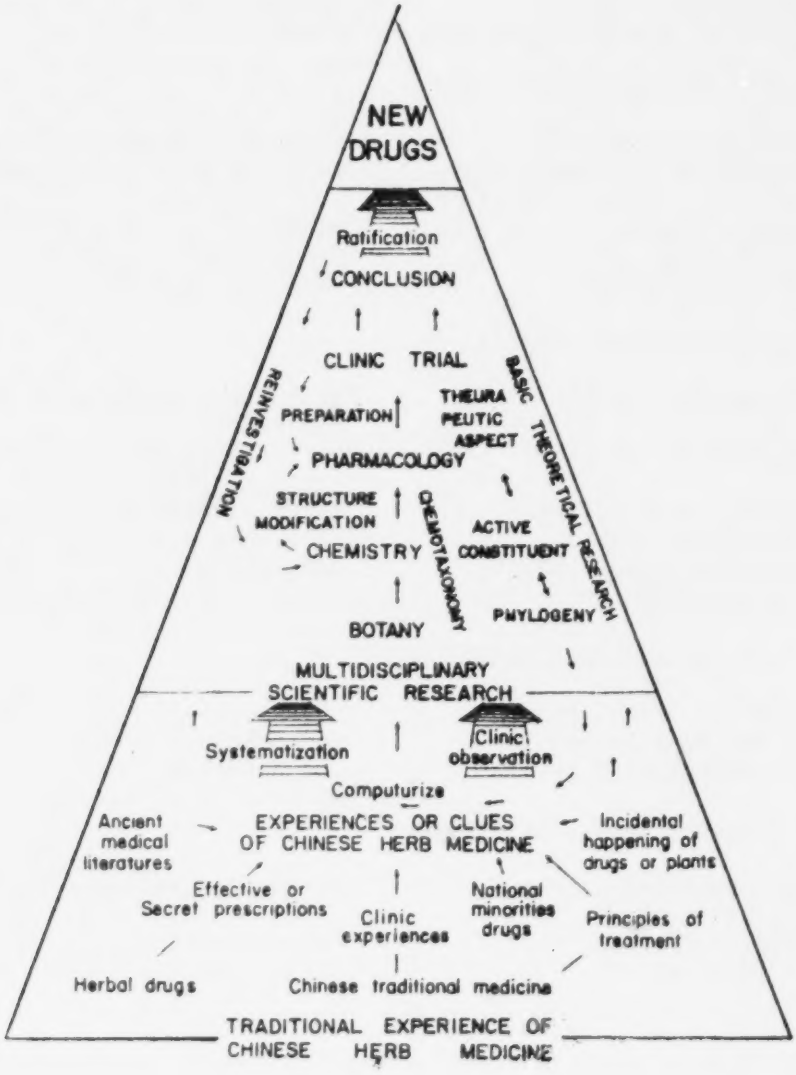

Figure I. Relationships among the traditional experiences of Chinese herb medicine, modern scientific research and new drug discovery

For the purpose of promoting and mobilizing Chinese traditional drug applications, application of modern scientific research methods is regarded as the best approach. The problem is, in the face of such vast possibilities, how best to identify the priority areas for research.

From the practical standpoint, drugs are sought that in primary health care and clinics show excellent therapeutic results. These are then investigated using multidisciplinary research - including pharmacognostical, chemical, pharmacological and clinical studies. After isolating and elucidating the chemical structure of the active principles, the chemical structures can be synthesized or modified so as to produce more favourable therapeutic agents. But while this is the generally accepted approach to drug research, the application of Chinese traditional drugs is usually in a compound prescription form that is determined under guidance of systematic principles and methods of treatment. Proper compatibility of drugs within a compound prescription may help increase therapeutic efficacy and decrease the side-effects or toxicity, if any. Of course, investigating compound prescriptions in connection with Chinese traditional medicine is much more difficult than for a single drug. Nevertheless, Chinese scientists are making more effort in this direction.

Medical experience teaches us to understand that traditional medicine is an important source for discovering new drugs. Since traditional drugs have been used for centuries and tested by billions of people, there has been ample opportunity to find satisfactory therapeutic agents and to solve problems of toxicity and side-effects. Based on rough statistics, 104 new drugs have been developed since 1949, of which about 60 relate directly or indirectly to Chinese traditional drugs.[7] The increasing emphasis on the use of traditional medicine in searching for new drugs in China is therefore the correct strategy.

There is a surprising amount of information on the experience of traditional medicine (ethnopharmacological applications) throughout China. Over the past twelve years the Institute of Materia Medica has collected 30,000 such items of information. On this basis, interdisciplinary systematization helps predict the most promising candidates for further laboratory and clinical investigation. Computerization seems to be best for this purpose and the Institute has recently started such work [8].

One important and interesting group of Chinese traditional drugs in the great treasure house of Chinese traditional medicine, are the tonics. The use of this kind of drug in China can be traced to the remote past. Already 2,000 years ago, the oldest Herbal Shen Nong Ben Cao Jing (Shen Nong Materia Medica) recorded 365 drugs and classified them into three functional categories - superior, medium and inferior. The superior category comprised 120 non-toxic drugs to be used for conservation of health, from which many drugs with tonic action have since been found - Panax ginseng and Acanthopanax senticosus being good examples. In the light of modern scientific research, more and more scientific data have demonstrated the beneficial action of tonics to the human body, for instance, the protein biosynthesis stimulating factor in Panax ginseng, the adaptogenic action (i.e. the ability to overcome small deviations and return body systems to normal) of Panax ginseng and Acanthopanax sentisosus, the induction of liver cytochrome P-450 to increase liver detoxicating action by Schizandra chinensis and Ganoderma capense, and the immunostimulating action of Astragalus membranaceus var. mongholicus and Acanthopanax senticosus. Tonics may thus be expected to become a vigorous field of development in pharmacy and pharmacology [9].

Conclusion

Chinese traditional drugs have already made and will continue to make a great contribution to the health care of the Chinese people. Furthermore, the experience of Chinese traditional medicine (ethnopharmacology data) offers a fundamental basis for research into new drugs.

Currently there is increasing emphasis on natural products for medicinal use all over the world. Traditional drug applications will certainly be further developed and flourish as a result of close international co-operation and mutual support.

Further reading

For additional information on modern developmenrts in Chinese traditional and herbal drugs, the reader is referred to references [10-12].

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Annex

Active principles isolated from Chinese traditional drugs

Qinghaosu	Daidzein
Agrimorphol	
Tetramethylpyrazine	
Sodium tanshinone II_A sulphonate	Gastrodin
Tutin	Gossypol
Yuanhuacine Anisodamine	
Anisodine	
Oridonine	Ponicidine
Curcumol	Curdione
Sarmentosine	Farrerol
Rorifon	Methylhydroquinone
5,7,3',4'-tetrahydroxy-flavane-3-nol c_4-C_8 dimer	Yingzhaosu A
Nevadensin	
Cryptotanshinone	Chuanliansu
Diallyl thiosulphonate	

TRADITIONAL CHINESE DOSAGE FORMS AND THEIR MODERNIZATION

By Hu Changhong*

A B S T R A C T

This article briefly explains Chinese traditional dosage forms, various kinds of which were evolved and applied in practice long ago. Ben Cao Gang Mu, (Compendium of Materia Medica) in the Ming Dynasty compiled almost all known dosage forms. Both the theory and technology of medicinal preparations were therefore well developed in ancient times. Since the founding of New China, a large amount of research work on Chinese traditional dosage forms has been carried out using modern techniques and methods. Many new dosage forms have been developed along with some rules about a more effective quality control.

This first part of the paper discusses the traditional dosage forms most in use, with emphasis on the techniques, actions and characteristics of honeyed pills, watered pills, pasted pills, waxed pills and plasters. The second part explains the improvements in traditional dosage forms and application of modern scientific techniques. According to the needs of clinical applications, new dosage forms of traditional herbal drugs have been designed, such as granular extracts, tablets, microcapsules, membranes, oral liquids, injections, suppositories, aerosols and adhesive plasters.

Traditional Chinese dosage forms

As recorded in Huangdi Neijing, (one of the extant ancient medical classics, ascribed to the ancient Emperor Huangdi (1698-2585 B.C.), traditional Chinese dosage forms such as decoctions, wines, pills, powders, potions, extracts and ointments were developed and applied long ago. In the Ming dynasty, the book Ben Cao Gang Mu (1596) written by Li Shizen recorded almost all known dosage forms, including those for oral administration, external application and otolaryngological treatment. The medical literature of ancient China explains that "in accordance with properties of drugs and symptoms of diseases, a suitable dosage form should be selected - pills, powders, decoctions, liquors or extracts", that "decoctions should be used for emergent cases, powders for slight chronic cases and pills for prolonged cases", and that "wines might keep the pathway of blood vessels free". What these theories and practical experience show is that dosage forms should be selected in the light of clinical applications.

Traditional Chinese dosage forms may be divided into two types - liquids and solids (including semi-solids). Liquid preparations take the form of decoctions, potions, liquors, aromatic waters, emulsions, syrups or fluid extracts for oral administration, and lotions, liniments, enemas, drops (drops

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*Professor, Institute of Materia Medica, Zhejiang People's Academy of Experimental Hygiene, Hangohn, Zhejiang.

for eye, ear and nose), mouth washes, inhalations, pigments and medicinal baths etc. for external application or otolaryngological treatment. Solid and semi-solid preparations take the form of powders (including those absorbed sublingually), cachets, pills, dry extracts, pastilles and medicinal preparations for oral administration, ointments, pastes, plasters, external powders (including snuffs, insufflations and dusting powders), suppositories (including bougies and pessaries) and cataplasmas (poultices) etc. for external application or otolaryngological treatment (including mucocutaneous application). All dosage forms except injections and tablets, the production of which had to await the development of the modern pharmaceutical industry, were prepared and applied in China before the Middle Ages.

Already in ancient times there were many improvements in the technology of the different preparations. For example, in preparing pills, there were both theories concerning their slow action and also considerable understanding of the effects of various adjuvants or excipients - pasted pills, for example, "are taken for being slow to disintegrate and waxed pills for being difficult to disintegrate". It was clearly understood in other words that the speed of release and absorption of a dosage form might be influenced by the selection of adjuvant or excipients.

In recent years, controlled experiments on model traditional preparations such as watered pills, honeyed pills (or bolus), pasted pills and waxed pills gave the accumulated release percentages of the main ingredients (as measured in vitro) shown in figure 1. This indicates that the watered or honeyed pills released their ingredients relatively rapidly while the pasted pills were slow and the waxed pills (with a release of less than 20 percent in six hours) were very slow, producing prolonged action. Such results are in agreement with experience using traditional preparations.

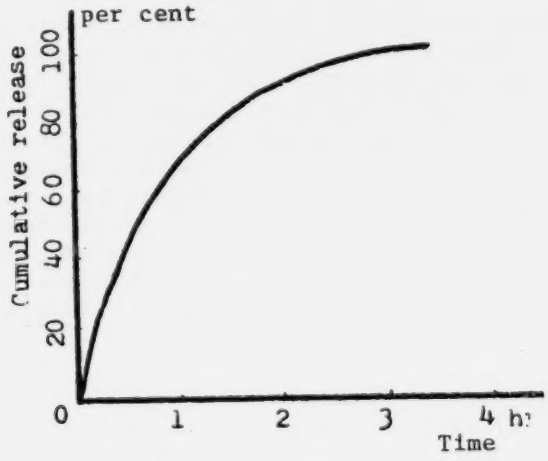

Figure 1. Cumulative-release curves of sulphanilamide in different pill forms

Likewise in processing traditional ointments and plasters for external application, classical pharmacy paid due attention to the selection of base material and processing technology. In ancient China, grease (animal fats), vegetable oils or a mixture of ingredients such as lard, sheep or ox fat, marrow, cheese, beeswax, sesame oil, rape oil, tung oil, tallow tree oil etc. were all used as ointment bases. In processing plasters, traditional Chinese drugs were first immersed in vegetable oil for three days, then heated at a higher temperature until the drugs began to shrink, and then filtered with thin tough silk. Lead oxide such as litharge, yellow lead or basic lead carbonate was then added to the hot oil filtrate. The mixture was then heated to such an extent so that it could form globules when dripped into water. It was then transferred to a container where it was treated with water for three days to remove so-called fire toxins (irritant artefacts). In effect this is a process for extracting oil-soluble ingredients: the plaster so prepared would act by penetrating the texture and becoming absorbed through the skin.

Recently, a comparative study on traditional Chinese plaster and modern adhesive plaster, both containing NaI^{131}, was made on animals. The results (figure 2) indicate that both plasters may release I^{131} - to be taken up by the skin - but the traditional dosage form is better.

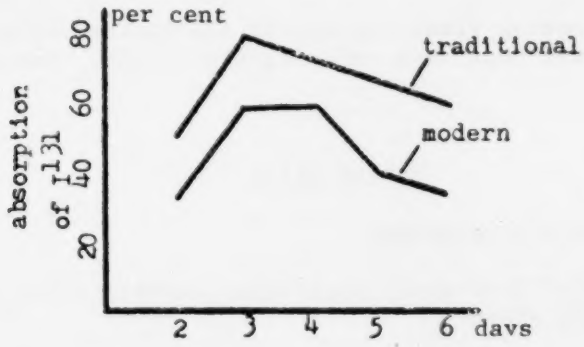

Figure 2. Comparison between traditional and modern plasters

Today, a great variety of traditional Chinese formulations in the form of decoctions, pills, powders, pastilles, extracts, aromatic waters, liquors, gelatins and plasters are still widely used and produced for medical application by China's pharmaceutical industry.

The main dosage forms come in four varieties - honeyed pills, watered pills, pasted pills and waxed pills respectively.

Four types of pills

Honeyed pills

Angong Niuhuang Wan (pills of Bezoar Resurrection)

The pills are prepared from Calculus bovis, Margarita, Cornus rhinoceri, Moschus, Borneolum, Realgar, Radix curcumae, Fructus gardeniae, Radix scutellariae etc.

Cornus rhinoceri is filed to a fine powder, Calculus bovis and Margarita are ground to very fine powders, medicinal plants such as Radix curcumae are ground into powder, and then evenly mixed and sifted. The powders are processed into 3 g pills with honey, covered with gold foil and sealed tight with a wax shell.

Treatment: for heat-clearing, detoxifying, and tranquilizing. Dosage: 1 pill, 1-3 times daily.

Watered pills

Muxiang Binglang Wan (pills of aucklandiae and arecae)

The pills are prepared from Radix aucklandiae, Semen arecae, stir-baked Fructus aurantii, Pericarpium citri reticulatae viride (stir-baked with vinegar), Rhizoma sparganii, Rhizoma zedoariae, Cortex phellodendri, Rhizoma coptidis, Radix et Rhizoma rhei, stir-baked Semen pharbitidis, and Mirabilitum depuratum.

The above drugs are ground into powders, sifted, mixed and then stirred evenly before being processed into pills with a water sprinkle and dried.

Treatment: for promoting vital energy circulation and eliminating stagnation, removing "evil heat" and relaxing the bowels. Dosage: 3-6 g, 3 or 4 times daily.

Pasted pills

Kongxian Wan (phlegm-dispelling pills)

The pills are prepared from Radix euphorbiae kansui (using vinegar), Radix knoxiae and Semen sinapis albae.

Radix euphorbiae kansui and Radix knoxiae are ground to powder, sifted, mixed and stirred evenly. A suitable amount of rice flour is mixed with hot water to form a paste, into which the above ingredients are mixed to form pills.

Treatment: for dispelling phlegm and removing retained fluids; also effective in treating hypochondriac pain.

Waxed pills

Weixi Wan (vital energy-strengthening pills)

Poria is decocted with Polyporus umbellatus, the dregs of which are removed. The remaining poria is then dried in the sun and ground into fine powder. An equal amount of Cera flava is melted over a water bath and while hot added to the poria powder and mixed. The mixture is then processed into 0.2 g pills.

Treatment: for lack of vital energy and kidney asthenia, and damp-heat accumulating in urinary bladder. Dosage: 9 g, chewed when the stomach is empty.

Other dosage forms

Other dosage forms in current use are summarized in the table below.

Other typical dosage forms, examples and main uses

Dosage form	Drug name	Main use
Powders	Zixue Dan	Dispelling fever - toxicity
	Xilei San	Dispelling toxins; healing abscesses
	Bingpeng San	Borneol and borax as anti-inflammation and analgesic agents
Pastilles	Limahuidin Dan	Treating boils
	Zijin Ding	Treating acute conjunctivitis
Extracts	Shiquan Dabu Gao	General nourishment
	Yimucao Gao	Extract of Herba leonurus - for young mothers
Liquors	Yangxie Yufeng Jiu	Blood nourishment and rheumatism Medicated liquours of tiger's bones and flowering quince for rheumatism
Aromatic water	Jinyinghua Lu	Water from Flores lonicerae, to eliminate toxic heat
Gelatin	Lupi Gao	Donkey-skin gelatin to nourish blood and staunch bleeding
Plasters	Huoxie Zhentong Gao	Activating blood circulation and pain relief
	Goupi Gao	Dog-hide plaster for rheumatism

Although considerable attention has been paid to controlling the quality of traditional patent medicines, historical limitations on the facilities available meant that only sensory identification methods could be used for quality control.

In modern times, standards of medicinal herbs have been established. With traditional experiences as a guide, modern scientific techniques are used to study traditional dosage forms. Specifications for quality control have been worked out regarding viable microbial counts, heavy metal content, weight loss on drying and residue on ignition etc. as well as routine tests on dosage forms. Physical, chemical and biological assays or identification of chemical entities are also envisaged. Since most of the traditional dosage forms are compound formulations, only microscopical identification (identification of ingredients with a microscope) is feasible in most cases. Nevertheless, research work is under way to enlarge the scope for chemical detection. In addition, great attention has been paid to stability of the dosage forms. For example, aromatic pills of the more costly drugs are packed in sealed wax shells so that they can be kept for a longer time.

Using modern science to improve traditional dosage forms

Traditional dosage forms are often either inconvenient to make or difficult to take. For example, decoction of drugs usually has to be carried out immediately before administration. Also, traditional pills made of crude drug powders are generally too large. Clinical requirements therefore compel us to improve the existing dosage forms - to render them more effective, less bulky and more convenient to take.

Using modern scientific techniques, traditional dosage forms can be changed to give quick, enhanced or sustained action. Methods of preparing many basic patent medicines and recipes with proven efficacy can be improved. Application of medicinal chemistry and pharmacology permits reduction of some formulations to a compound of effective ingredients giving a new dosage form smaller in size, reliable in effect and convenient for administration.

Parameters for controlling drug contents can be investigated to ensure safety and efficacy. Quality control in fact becomes more and more important with the broadening scope of dosage forms and their new applications.

A great number of improved traditional dosage forms have been evolved by this means. The main ones - granules, tablets, microcapsules, membranes, potions, injections, suppositories, aerosols and adhesive plasters are described below.

Improved dosage forms

Granular extracts (granules)

Granular extracts evolved from decoctions but retained their characteristic of being rapidly absorbed. Freed from bulkiness and liability to deterioration the new dosage form is convenient to transport, store and administer. Generally, the granules are made, according to prescription, from extracts from the constituent drugs. Sugar, dextrin etc. are added as excipients.

The bitter taste of some drugs may be corrected by adding a larger amount of sugar. The granules so prepared are called "dry syrup", and are generally taken after being mixed with hot water. Another class of granules evolved from medicated liquors are prepared from alcoholic extracts, and are taken with the addition of spirit.

In general the granules should be sized by passing through sieves giving less than 5 per cent fine particles. Another quality criterion is that after being mixed with water and added to 20 volumes of hot water, the granules should be soluble after shaking. The variation in content in packages containing less than 10 g should not exceed ± 7 per cent; packages containing more than 10 g, should not vary more than ± 5 per cent.

Example 1: antipyretic granules for common colds - in the form of brown granules of sweetish bitter taste.

Method of preparation: isatis leaves and roots (200 g each), forsythia fruits and bistort rhizome (100 g each) are decocted twice with water. The decoctions are combined and filtered and the filtrate concentrated to specific gravity of 1.8. An equal amount of alcohol is added and, after sedimentation, the upper limpid liquor is separated and concentrated. After adding 1.5 volumes of water and stirring, the mixture is allowed to settle for eight hours and then separated. The upper limpid liquor is concentrated again to specific gravity of 1.38-1.40. Granules are made by adding one part of this concentrate to 2.5 parts sugar powder, 1.25 parts dextrin and an appropriate amount of alcohol. The granules are dried and packed into 16-g bags.

Actions and uses: elimination of heat-toxics, treatment of upper respiratory infections, acute tonsillitis and laryngopharygitis. It is taken after being made up with boiling water: 16-32 g at a time, three times daily.

Example 2: Yang Xie Yu Fen Jiu (a liquour granules) - in the form of yellow or brown granules, with aromatic odour, sweet and some bitter taste.

Method of preparation: preparation evolved from medicated liquors containing fifteen ingredient drugs such as eucommia bark, ledebouriella root, gentian root, white atractylodes rhizome, safflower, wolfberry fruit, Chinese angelica root, cythula root etc. These drugs are extracted with alcohol, processed to dry granules and taken with the addition of spirit.

The drugs are percolated with 50 per cent alcohol and the percolate condensed to a thick extract. Finely powdered sucrose is added, the mixture stirred evenly, flavoured and then prepared as granules. The granules are packed in 50-g bags.

Actions and uses: used to nourish blood, dispel pathogenic wind, and to treat rheumatism, numbness in limbs, and pains in sinews and bones. Each bag of granules is dissolved in 500 ml of liquor. Dosage: 15-30 ml at a time, 1 or 2 times daily.

Tablets

The tablets are mostly derived from traditional decoctions and pills. Their advantages are that they can easily be produced on a large scale, output is high and quality is easier to control. At present, they are mainly based on extracts of drugs and their active components. The tablets may be coated if desired.

Example 1: tablets of angelica - each sugar-coated tablet contains 0.25 g of extract, equivalent to 0.5 g of angelica root.

Composition and preparation: angelica root coarse powder is percolated with 70 per cent alcohol until the percolate becomes nearly colourless. The percolate is distilled to recover alcohol, firstly at atmospheric pressure, then under vacuum at temperatures below 65°C. After adding sufficient dextrin, Bolus alba and magnesium oxide and mixing evenly, the mixture is brought to dryness at a lower temperature. The mixture is taken out, rolled into small pieces and granulated with the addition of magnesium stearate and talcum powder as lubricants. At a relative humidity below 70 per cent, the granules are pressed into tablets then sugar-coated.

Actions and uses: used in treating menstrual disorders, dysmenorrhea, menorrhalgia etc. Dosage: 1 or 2 tablets each time, 3-6 tablets daily.

Example 2: tablets of lonicera and scutellaria - each tablet contains 0.1 g of honeysuckle flower and 0.08 g of baicalein.

Method of preparation: the extract of honeysuckle flower and baicalein are thoroughly mixed, sufficient quantity of starch is added, the mixture is moistened with alcohol and processed into granules. The granules are dried at under 60°C, pressed into tablets with the addition of a small amount of lubricant, and then sugar-coated.

Actions and uses: for eliminating heat-toxics and diminishing inflammation, for treating infection in the upper respiratory tract, and for acute tonsillitis and pharyngitis. Dosage: 2-3 tablets each time, four times daily.

Notes: baicalein is isolated from roots of Scutellaria baicalensis Georgi. The extract of honeysuckle flowers is prepared by decoction followed by preliminary purification with addition of alcohol. After sedimentation, the clear liquor is taken to dryness.

Example 3: tablets of berberine hydrochloride - the content of berberine hydrochloride ($C_{20}H_{17}O_4N.HCl.2H_2O$) in each tablet should be 93.0-107.0 per cent of the labelled amount, i.e. 0.1 g or 0.05 g.

Method of preparation: the berberine hydrochloride is mixed evenly with 10 per cent of its weight of starch mucilage to form a soft mass. It is then granulated and dried at 70°C to reduce the moisture content to about 6 per cent. Magnesium stearate, and the mixture is then regranulated and pressed into tablets. The tablets may be coated with a thin layer of zein to mask the bitter taste.

Actions and uses: antibacterial, used in infections of the gastro-intestinal tract. Dosage: 1-3 tablets each time, 3-9 tablets daily.

Notes: berberine hydrochloride is an alkaloid that can either by isolated from plants of berberidaceae or synthesized.

Microcapsules

Microencapsulation is a new technique in which the drug particles are coated with thin membrane to form sealed fine globules. This improves their stability and controls their rate of release. An example of its use to improve dosage forms of materials isolated from traditional Chinese drugs are microcapsules of agrimophol.

Agrimophol is the active compound isolated from the winter root of Agrimonia pilose ledeb. It possesses strong taeniafuge activity and is strongly hydrophobic. The disintegration and release characteristics of the tablet form were apparently poor. Microencapsulation of the compound increases both its stability and its dispersion rate, and improves its action in the gastro-intestinal system.

Method of preparation: microencapsulation is carried out by phase separation-complex coacervation:

(1) The preparation of emulsion: agrimophol crystals are ground and mixed with an equal amount of acacia powder, an appropriate quantity of 0.2 per cent sodium bisulfite solution (antioxidant) is added continuously to make the initial emulsion. After dilution, it is transferred into a tissue triturator to be processed at 8,000 rev/min for several minutes to prepare the emulsion.

(2) Complex coacervation: the emulsion is stirred evenly after adding to it an equal volume of 3 per cent gelatin solution which has been previously adjusted to pH 8.0. It is heated over a water bath after being diluted with its own volume of distilled water, then complex-coacervated with addition of 10 per cent acetic acid to pH 4.1-4.3 under slow stirring.

(3) Solidification: the complex-coacervated liquor is diluted with an equal volume of cold water, which brings the temperature down to 50°C. An appropriate amount of 37 per cent formaldehyde solution is added during stirring for 15 min, which hardens the encapsulation. The pH is then adjusted to 7.0 by adding 10 per cent sodium hydroxide solution. The mixture is stirred for a further 10 minutes, then transferred to a refrigerator. The microcapsules are collected by filtration and washed repeatedly with cold water to remove formaldehyde, then vacuumed to dryness.

(4) Granulation: a sufficient quantity of starch is added to the microcapsules and the mixture stirred and pressed through a screen to make the granules. It is then air-dried and passed through another screen.

Actions and uses: acts as a taeniafuge which causes lethal spasms of the scolex and body segment of tapeworms. In treating tapeworm infections it is administered as a single dose orally in the morning on an empty stomach. Dosage: 0.8 g for adults, 25 mg per kg weight for children; with a cathartic.

Notes: agrimophol may be assayed spectrophotometrically. The release rate in artificial gastric and intestinal fluid is shown in figure 3.

As shown in figure 3, the accumulative release of agrimophol is 70.5 per cent in the first hour and 91.9 per cent in the second. This seems to favour an action on tapeworms in the upper small intestine.

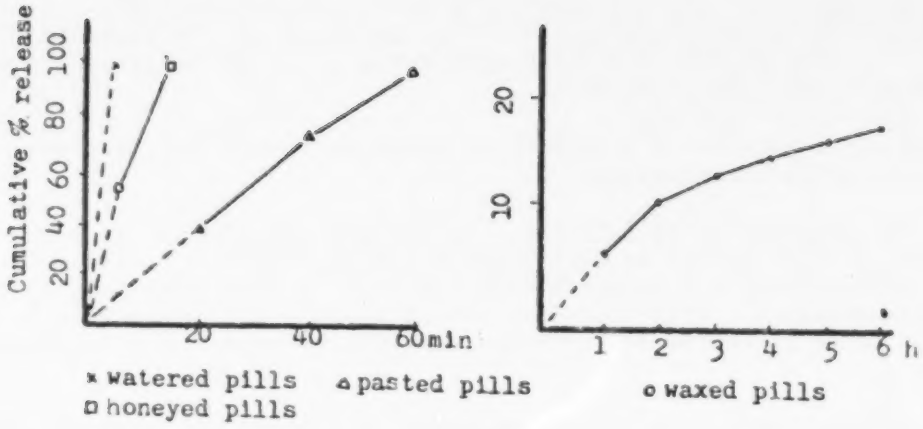

Figure 3. Agrimophol released from microcapsules

Membranes

Medicinal membranes are prepared by first dissolving or suspending the drug ingredients in membrane-forming material. The material is then spread into a membrane film, dried, assayed and divided into appropriate dosages. It may be administered orally (sublingually), used in the eyes, or on skin, mucosa and wounds. An example of a membrane containing active compounds isolated from traditional drugs concerns rhodein, a film-like preparation. Each piece contains 5 mg of rhodein, and may be administered sublingually.

Method of preparation: rhodein is a glycoside isolated from the root of Rhodea japonica rath; polyvinyl alcohol (PVA) is employed as the membrane-forming material with the addition of a little titanium dioxide, glycerin, Tween-80, edible pigment, flavouring agent and saccharin.

The PVA is immersed in distilled water, dissolved by heating over a water bath, and then filtered. After cooling, ground titanium dioxide is stirred in, followed by an alcohol solution of the rhodein, a small amount of glycerin, Tween-80, flavouring agent, edible pigment and saccharin. After settling to dissipate air bubbles, it is mechanically spread into the membrane, then dried.

After an assay of the rhodein content, the membrane is cut into lengths according to the required dosage. The membrane pieces are wrapped in coated aluminium foil and sealed.

Actions and uses: in strengthening heart functions, promoting diuresis, and for treating arrhythmia and tachycardia. Dosage: 5 mg of rhodein at a time, 3 times daily.

Potions

Potions are a dosage form that evolved from traditional decoctions. They are usually packed in single-dose ampoules to ensure storage quality. An example is Shen Mai Yin (oral liquid).

Method of preparation: made from Codonopsis pilosula root, Ophiopogon japonicus root and Schizandra chinensis fruit. A mixture of the drugs is decocted and filtered and the filtrate concentrated to a level equivalent to 2 g/ml of crude drugs. After cooling, 2 volumes of 95 per cent alcohol are added to precipitate inert substances. The mixture is filtered after 24 hours, then concentrated under reduced pressure. Simple syrup and sodium benzoate are added together with distilled water to make up to volume. It is then distributed into 10-ml ampoules and sterilized.

Actions and uses: to nourish Yin (vital essence) and replenish body fluid; in treating exhaustion of vital essence and difficiency of the lung orb etc. Dosage: 10 ml each time, 3 times daily.

Injections

Injections of traditional drugs are prepared mostly from chemically well-defined active principles or fractions, with the aim of quicker onset of action. An example is Leonurus.

A colourless, transparent and sterilized aqueous solution of pH 4.5-6.5 is prepared from the dry herb Leonurus artemia S.Y. Hu (syn. Leonurus heterophyllus) Sweet. It contains over 90 per cent of labelled amount of total alkaloids calculated as stachydrine hydrochloride ($C_7H_{13}O_2N.HCl$).

Method of preparation: defined amount of coarse Leonurus powder is percolated with alcohol containing 0.1 per cent sulphuric acid overnight. The percolate is collected and concentrated, then melted with a little paraffin. The paraffin is then separated. After basification, the percolate is extracted repeatedly with chloroform. The solution is then heated to remove all traces of chloroform. The pH is adjusted to about 5 and the solution filtered. After adding 1 per cent benzyl alcohol, the content of total alkaloids is determined, then adjusted with water so that each ml of injection contains 20 mg total alkaloid. The injection solution is then filtered through a membrane, distributed into ampoules and sterilized.

Actions and uses: for inducing uterine contraction, staunching uterine bleeding and regulating menstruation. Dosage: for intramuscular injection, 1 or 2 ml each time, 1 or 2 times daily. Not to be used for pregnant women.

Another example is injections of Pueraria flavones, a transparent sterilized aqueous solution containing in 2 ml (100 mg total flavones) of Puerariae lobatae.

Method of preparation: a calculated amount of the total flavones is dissolved in normal salt solution by heating. After adjusting the pH to 6.5-7.0, the solution is left in a refrigerator for two days and filtered, then distributed into ampoules.

Actions and uses: to treat coronary heart disease and abrupt deafness.
Dosage: for intramuscular injection, 1 or 2 ml each time, 1 or 2 times daily.

Notes: Pueraria lobata belongs to Leguminosae; its dry root contains mainly isoflavones diadzein, daidzin and puerarin etc.

Suppositories

Suppositories are a form of dosage of ancient Chinese origin. However, it also appears in a refined dosage form with formulations derived from medical herbs. Examples are suppositories of Cnidium and Coptis.

Method of preparation: made of finely powdered Cnidium fruit and Coptis root with the addition suitable quantities of boric acid and glucose. The ingredient drugs are mixed together with a small amount of glycerin to form paste. This is added to molten glycerinated gelatin (the suppository base) over a hot water bath. It is then evenly mixed and poured into a lubricated vaginal suppository mold.

Actions and uses: in the treatment of vaginal trichomoniasis.
Dosage: one suppository daily.

Notes: glucose serves as an in situ organic source of lactic acid. Both the boric acid and glucose produce an acidic vaginal environment (pH 3.8-4.4) that checks the growth of protozoa, and restores the normal biological state of the vagina.

Aerosols

Aerosols containing traditional drugs are used for inhalation or for local application, for example the aerosol of argyi oil prepared from an alcoholic solution of argyi oil together with a suitable propellant. The argyi oil in each package should not be less than 2.7 ml.

Method of preparation: argyi oil, a small amount of lemon essence, and an alcoholic solution of sodium saccharin are mixed in a specially designed aerosol container and sealed. It is then pressure-filled with sufficient difluoromethane (Freon-12) as propellant.

Actions and uses: effective in relieving asthma, easing coughs, dispelling phlegm and resolving inflammation; it is used in treating chronic bronchitis, pulmonary emphysema and bronchial asthma. It may be inhaled three times daily.

Notes: argyi oil is a volatile oil obtained from dry leaves of Artemisia argyi Levl. et Vant. (compositiae) by steam distillation.

Medicated adhesive plasters

These are an improved dosage form based primarily on traditional plasters. The rubber, as the main base, is mixed thoroughly with resin, fat or lipids as adjuvant, and powdered drugs or extracts of drugs. It is then spread on cloth or other suitable materials. The components of the plaster are stable. It has a strong adhesive power and can be applied directly without being heated. An example is Shangshi Zhitong Gao, an adhesive plaster for rheumatic pains. A pale green coloration is visible on the plaster surface and it has an odour of wintergreen oil.

Method of preparation: made according to a formulation comprising 16 medicinal herbs such as Darallia rhizome, aconite root (Sichuan aconite root), Aconite kusnezoffii root (wild aconite root), Nux vomica, and six other ingredients such as extract of belladonna, extract of ruta, wintergreen oil, peppermint oil, camphor and borneol.

Preparation is effected in four stages:

(1) The medicinal herbs are reduced to coarse powders and extracted with alcohol by percolation. The percolate is collected and concentrated to a thick mass;

(2) The plaster base is made by pressing rubber into thin flakes and then immersing them in gasoline. After dissolution, the mixture is transferred to a rubber mixer and a prescribed quantity of vaseline, wool fat, zinc oxide and powdered rosin are added as the adjuvants while stirring;

(3) The medicating ingredients are added to the base, and mixed thoroughly to give a semi-solid medicated adhesive mass;

(4) The adhesive mass is spread onto cloth using a spreading machine. It is then covered with a layer of hard gauze or plastic film. It is finally cut into pieces (5 x 7 cm) dimension so that the adhesive mass on each piece is not less than 0.6 g. When tested by heating to 120°C for 30 min the back surface of the plaster should not show any sign of oil permeation.

Actions and uses: the plaster assists in dispelling pathogenic wind and dampness, and in eliminating blood stasis and relieving pains. It is used to treat rheumatic and other pains, injuries caused by falls, fractures and strains. It is not to be used by pregnant women.

Notes: tests showed that medicated adhesive plaster has almost the same penetrating power through skin as that of the traditional plaster (see figure 2). It is simpler to make and easier to use.

DEVELOPMENTS IN INDUSTRIAL PRODUCTION OF CHINESE TRADITIONAL AND HERBAL REMEDIES

By Liu Deyan*

A B S T R A C T

Production of Chinese traditional and herbal medicines has three aspects: the drug collection, crude drug processing and preparation of dosage forms. In earlier times most crude drugs were gathered from the wild. They were processed and compounded manually in workshops by primitive means. Rapid development in production was therefore impossible owing to the limited supply of raw materials and dependency on manual operation.

Since the founding of the People's Republic several measures have been taken to promote the following aspects of production: (a) cultivation of medicinal plants and domestication of medicinal animals; (b) innovation of traditional methods for crude drug processing in order to adapt them to the requirements of mechanization; (c) modernization of the equipment to serve the purposes of industrial production and (d) standardization of processing procedures to ensure quality control. As a consequence, the production of Chinese traditional drugs exhibited an 8-fold increase in sales during 1956 to 1981, compared to 25-fold increase in ready-made dosage forms.

Three suggestions to ensure further advances in the field are (a) speeding up construction of bases for cultivation and breeding, (b) developing new formulations with specific therapeutic effects, and (c) adopting modern technology and equipment in production.

Production of Chinese traditional drugs covers plant cultivation and animal breeding, collection and processing of crude drugs, and final preparation of dosage forms and compound formulations. After being processed, the crude drugs are usually sliced to yingpian, a ready-made form used directly for decoction. In addition, they may go into various formulations, such as pills, powders, soft extracts, plasters, troches (lonzenges), liquors, pellets and medicated teas.

Being endowed with abundant resources, China has a long history in the production and application of a great variety of traditional drugs. Effective application of them over thousands of years has been acknowledged both domestically and abroad. Nevertheless, before liberation, owing to the restrictive policies of the pre-revolution Government, the production of traditional drugs was not well developed.

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*Liu Deyan (Ms.), Engineer, State Pharmaceutical Administration of China, Beijing.

Cultivation of medicinal plants was carried out by peasants on an individual basis; pharmaceutical preparations were made manually in workshops with only very primitive facilities.

Ever since the foundation of the People's Republic, the Party and Government have paid great attention to promoting Chinese traditional medicine and to producing traditional drugs. The drugs were procured and supplied according to plans and the development in production was tremendous. Comparing sales figures for 1981 with those in 1956, there was an 8-fold increase in overall sales and a 25-fold increase in ready-made dosage forms. Research on traditional drugs has made great strides, in (a) cultivation of medicinal plants and farming of medicinal animals, (b) processing crude drugs, (c) development of new dosage forms and compound formulations and (d) improvement of production facilities and quality control of crude drugs and formulations.

Production of crude drugs

The total number of Chinese traditional and herbal drugs as recorded in formal literature is estimated to be over 5,000, of which vegetable drugs are the majority (90 per cent) followed by drugs of animal and mineral origin. They comprise (a) 1,000 drugs marketed and sold in drug stores, of which 600 are in common use, (b) a further 500-600 minority drugs, and (c) herbal drugs used occasionally in folk medicine.

In the past, the majority of crude drugs were gathered from the wild; only a few were obtained by cultivation or artificial breeding, and some had to be imported. After liberation, the rise in living standards meant that the then-existing production methods could not meet the needs of people - natural resources of medicinal plants and animals are limited and excessive exploitation has already produced signs of exhaustion. For instance, indiscriminate digging of barberry root (sankezhen or Berberis soulieana), used as raw material for berberine extraction, has severely depleted the resource. Similarly, musk deer, the source animal of musk, is now on the verge of extinction due to over hunting. In view of this, the State Council issued a directive in 1958 to speed up development of collective medicinal plantations. Five million mu* of arable and nonarable land were allocated by the State for growing medicinal plants. Measures were also taken to encourage individual peasants to take part in the project. The number of medicinal plants cultivated in large quantities has reached around 150. Some animal species of medicinal interest have also been domesticated.

Cultivation of medicinal plants

Some 70-80 per cent of Chinese drugs are still collected from the wild. Their output is unstable and cannot be raised at will. In order to raise and stabilize output, and improve the quality of crude drugs, artificial cultivation has been systematically investigated. As a result some species of wild plants, e.g. Aucklandia (muxiang, Aucklandia lappa) star anise (baj. muixiang, Illicium verum), gastrodia (tiama, Gastrodia elata) are now cultivated.

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*1 mu = 0.0667 hectare.

Domestication of animals

Animal drugs play an important role in traditional therapy; breeding farms to supply their raw materials have been set up in many regions. For example, pilose antlers, produced by the breeding farms in the north-east and south now account for more than 80 per cent of commercial supply of the drug derived from them. Production of pearls by artificial cultivation has succeeded in Shanghai, Jiangsu, Hunan, and Guangxi, resulting in better supply of medicinal pearls. Experimental domestication of musk deers has been carried out in Sichuan, Shanxi and Anhui with encouraging results. Wingless cockroaches (tubiechong, Eupolyphaga sinensis) have also been successfully raised artificially.

Introduction of exotic medicinal plants into plantations

Previously, some sixty exotic traditional drugs were only available as imports. By introducing these plant species into plantations, more than twenty have been successfully grown in China. The main items are amomum, cinnamon, cloves, aucklandia, nutmeg and senna.

Based on phytogenetic relationships, a number of indigenous plants were investigated as alternatives to those imported. Some products with similar therapeutic activity have been found in this direction. A number (see table 1) have been included in the Pharmacopoeia, (1977 ed.).

Table 1. Examples of indigenous substitutes for imported drugs listed in The Chinese Pharmacopoeia

Chinese name	Botanical origin	
	Imported drugs	Indigenous substitute
Chenxing	Aquilaria agallocha	A. sinensis
Maqian	Strychnos nux-vomica	S. wallichina
Anxixiang	Styrax benzoin	S. hypoglauca
Awei	Ferula asafoetida	F. sinkiangensis
Luhui	Aloe vera	A. vera var. Chinens
Luofumu	Rauwolfia serpentina	R. verticulata R. yunnensis

Survey of drug resources for exploitation

Source plants with high contents of active principles or valuable chemical constituents are constantly surveyed for potential exploitation. For example, ephedra species was surveyed as sources of ephedrine alkaloids, especially the now more valuble (+)-Ψ-ephedrine; the Dioscorea species was surveyed for diosgenin. Those selected were subjected to further studies and propagation.

Development of artificial cultures for the production of fungal drugs

Large-scale culture techniques in connection with antibiotic production have been intensively studied in recent years. It was also reasoned that similar technology could be adopted for producing traditional drugs of fungal origin. Both submerged fermentation and solid bed culture techniques have been developed, making large scale production feasible. Successful examples (see table 2) are glossy ganoderma (lingzhi, Ganoderma lucidum), poria (fuling, Poria cocos), ergot (maijiae, Claviceps microcephala) and liongjun (Armillariella tabecens).

Table 2. Fungal drugs successfully produced using artificial cultures

Name of the fungal drugs	Culture method
Glossy ganoderma (lingzhi)	(1) Solid bed in bottles (2) Submerged fermentation
Poria (fuling)	Artificial culture on pine wood chips
Ergot (maijiao) (Claviceps purpurea)	Submerged fermentation of C. microcephala to produce ergometrine
Liongjun	Submerged fermentation of Armilariella tabescens

Processing of crude drugs

For convenience of storage and transportation and in order to meet dispensing and compounding requirements, natural materials collected have to be processed in a variety of ways to give different forms of crude drugs. Processing may involve physical operations as well as chemical or biochemical treatment of the natural material. During processing, crude drugs are broken up into small pieces or cut into chips or slices (yinpian) that can be readily dispensed for decoction. The objectives in the processing of crude drugs are (a) to remove mud, other foreign matter and any parts not used in medicine, (b) to reduce or eliminate toxic or unwanted effects, (c) to enhance therapeutic efficacy, (d) to correct unpleasant odour or taste and (e) to render the material more easily pulverized. The established procedures may include besides cleansing and volume reduction, operations such as baking, steaming, boiling, maceration, simmering over a water bath, roasting or calcination.

Processing of crude drugs constitutes an important part of Chinese pharmaceutical production. Because of this a large amount of research work has been carried out during the past thirty years in order to improve the various processes and to elucidate the principles concerned. Although it was found that the traditional methods of processing were generally rational, studies were made to improve them and to make them more adaptable to mass

production and modern technology. Progress in this respect includes elucidation of the principles involved, innovations in traditional processing, mechanization and semi-automation of processing and standardization of processing techniques.

Elucidation of principles

Principles involved in the traditional methods may be summed up according to the chemical reactions that may possibly occur during the processing of the crude drug.

Crude drugs containing alkaloids

Many Chinese drugs depend on their alkaloid content as their active principles. For instance, coptis root (huanglian, Coptis chinensis), berberis root (sankezhen, Berberis sargentiana) and phellodendron bark (huangbei, Phellodendron chinense and P. amurense) all contain berberine; corydalis tuber (yuanhu, Corydalis yanhusuo) contains yanhusuo alkaloids. Since most alkaloids are not easily soluble in water, vinegar treatment in traditional methods of processing may be interpreted as intending to render the alkaloids present more soluble. For example, during stir-baking Corydalis tuber with vinegar, forms more-soluble acetates of yanhusuo alkaloids. Furthermore, alkaloids in natural state are usually coupled with tannins, oxalic acid etc. in the form of insoluble complexes. Vinegar treatment may set them free and turn them into soluble acetates as above.

Crude drugs containing glycosides

The Chinese drug evergreen (wannianqing, Rhodea japonica) contains cardiac glycosides; bitter almond and peach kernel contain amygdalin; polygala (yuanzhi, Polygala tenuifolia and P. sibirica) and balloon flower root (jiegeng, Platycodon grandiflorum) contain saponins; and sophora flower (huaihua, Sophora japonica) contains flavonoid glycosides. Alongside the glycosides many of these crude drugs contain enzymes that can hydrolyse the glycosides into sugar components and aglycones, thereby destroying their therapeutic activity. Some processing conditions can destroy the enzymes and thus protect the activities of the drug. Bitter almond is an example, processing of which by steaming or boiling inactivates emulsin. The processing of sophora flower has a similar effect.

Crude drugs containing volatile oils

Normally it is obvious that a crude drug containing volatile oil such as peppermint, schizonepeta (jingjie, Schizonepeta tenuifolia), asarum herb (wild ginger, xixin, Asarum heteropoides) or cinnamon bark (guipi, Cinnamon japonica) should not be heated during processing. But in some cases, where a highly volatile oil would cause irritation, heat treatment is applied to eliminate the more volatile constituent. An example is stir-baking of aucklandia root (muxiang, Aucklandia lappa). Similarly, some crude drugs are gently heated with an absorbent, such as stir-baking of atractylodes rhizome (cangshu, Atractylodes) with ash.

Crude drugs containing organic acids

Generally, organic acids exist as insoluble calcium salts. Vinegar treatment in those cases may therefore serve to convert the calcium salts into soluble free acids. The processing of black plum (wumei, Prunus mume), schisandra fruit (wuweizi, Schizandra chinensis), Chinese ilex fruit (dongqingzi, Ilicis pedunculasae) are examples.

Innovation in traditional processing techniques

In order to adapt to the needs of industrial production, traditional technology for processing crude drugs has to be improved or changed. Progress in this direction is illustrated by the following examples.

(1) Pressurization during maceration at room temperature. Texturally very tough drug raw materials have to be softened by water maceration before cutting. Formerly, this was a time-consuming process requiring three to fifteen days. Pressurization (up to 10 atm) of the process may significantly shorten the time greatly (e.g. to less than 26 hours). Typical Chinese drugs such as the Chinese yam (shanyao, Dioscorea opposita) in hard lumps with a powdery texture, chuangxiong (Ligusticum chuanxiong) which is oily in texture, and betel nut (areca seed, binglang, Areca catechu), have been experimentally treated with this modified maceration process and gave a 84-99 per cent time saving.

(2) Use of enzymatic degradation techniques. In processing tortoise shell (gui-ban), turtle shell (bie-jie) and ass skin (lu-pi) enzymes remove remnants of animal tissues within three to ten days. In the traditional process the materials would have to be left in water for forty to fifty days.

(3) Detoxification of aconite. The traditional process involved tedious soaking in water and boiling with liquorice over a period of about fifteen days. Since the intention was to convert the highly toxic aconitine to less toxic aconine, a modified process which involves heating on steam bath under 1.5 atm pressure for 90 minutes saves both time and labour, and gives better quality control.

(4) Processing of pinellia tuber. The traditional maceration process for pinellia tuber (banzia Pinellia ternata) necessitated soaking in water with daily replenishment until disappearance of an astringent taste. This was usually after fifteen to forty days. A new processing technique is now available in which the raw material is heated in an autoclave at 115°C for two and half hours. This removes the toxic principles without significant loss of the active principles.

Mechanization and semi-automation of processing operations

Traditional processing of crude drugs has for the most part been carried out manually. In recent years various machines and equipment have been introduced or designed and built for mechanization of those operations. These are described in more detail in the next section.

Standardization of processing procedures

Although the development of traditional processing technology for crude drugs has a history of more than a thousand years in China, because of differences in medical practice and other reasons, the methods tend to vary from place to place. Thus a crude drug might not be identical in quality when obtained from different parts of the country. Measures have therefore been taken to unify processing procedures. The general rules for processing are given in the 1977 edition of the Chinese Pharmacopoeia along with specifications and processing procedures for each drug. However it is understandable that traditions formed in the long past are not easily changed. Further work is needed to speed up progress. In this connection chemical, pharmacological as well as technological improvements in processing are needed. The laboratory studies are underway in several of China's institutions.

Production of dosage forms and compound formulations

Descriptions of the art of compounding date back to earliest records of drugs. The various dosage forms designed to facilitate administration according to therapeutic requirements also appeared in early history. However it was during the Song dynasty that standardized preparations of drugs came into being. By then the State monopolized the drug trade and drugs, dosage forms and compound formulations were prepared and sold officially. National formularies were also published. Nevertheless, the development of traditional medicine in old China was limited by the feudal economy. The state of the art in fact remained almost the same until liberation.

The dosage forms and compound formulations of traditional remedies prior to liberation had the following shortcomings: (a) production was carried out in small workshops attached to drug stores; (b) production facilities were simple: most of the work was done manually and productivity was low; (c) dosage forms were relatively limited and not suited to the requirements of contemporary life; and (e) lack of unified specifications made the standardization and quality control of products extremely difficult.

Following the foundation of the People's Republic, great effort has been made to: (a) reform the production structure so that small workshops developed into factories; (b) mechanize and semi-automate manual operation; and (c) increase dosage forms and specifications, and improve product quality.

Reforming production structure

As noted above, in old China, traditional Chinese dosage forms and compound formulations were prepared only manually in backyard workshops. However, after liberation, especially during the socialist transformation period, small workshops were amalgamated into factories that were entirely devoted to drug production. This opened the way to further development as illustrated by the Wuhan Zhonglian Pharmaceutical Factory. The enterprise was first established in 1952 by merging 190 backyard drug store workshops. It started to make rapid advances following a switch to joint state-private ownership in 1955. Now, it has about 1,000 workers and has become one of the largest traditional pharmaceutical factories.

In implementing the State Council Directive No. 121 of 1973, comprehensive technical reform of traditional pharmaceutical factories started all over the country. Factory workshops were updated, and a number of new and modern workshops were built using investments from the State. Through the reform,

reorganization permitted specialization and co-ordination. Factories were enlarged and productivity raised. In Tianjin, for example, nine factories under the Municipal Traditional Pharmaceutical Cooperation were co-ordinated in an overall plan. Each factory is assigned to specialize in one or two dosage forms, while continuing with other minor varieties. Thus, the No. 1 Tianjin Traditional Pharmaceutical Factory specializes mainly in tablets and ampoules; the No. 2 Factory in honeyed bolus and medicated liquours; the No. 3 Factory in various forms of pills; the No. 4 Factory in plasters; the No. 5 Factory in powders and so on. Specialized production brings to a factory the possibility of developing faster, better and more economically.

Modernization of equipment

In the past, equipment used to process and compound Chinese drugs was very simple, and manual operating conditions could hardly conform to hygienic requirements. Increasing demand for traditional remedies, production of new dosage forms and better quality control, all stressed the importance of modern equipment and technology.

Equipment required to produce Chinese traditional remedies can be divided into three categories: (1) to process crude drugs, (2) to extract and separate active constituents, and (3) to compound ingredients into final dosage forms and packaging. In order to meet the varied needs, ready-made machines and apparatus such as pulverizers, extractors, evaporators, clarifiers etc. have been introduced from other industries. At the same time modified or novel equipment was designed and tailor-made to the specific requirements of crude drug processing and for producing dosage forms and compound formulations. The honeyed bolus machine is one example. Other equipment with unique features is listed in tables 3, 4, 5. Other machines and apparatus are under design and testing, e.g. a drug grading machine, a honey processing equipment, a kneading machine, a honeyed-pellet machine and a plaster processing machine.

Table 3. Equipment for processing crude drugs

Equipment name	Function and application	Type
Drug washing machine	Cleaning away mud and washable foreign matter; reducing the bacteria count	(1) Rotary drum (2) Screw-type conveyer
Drug cutting machine	Softening the crude drug, then cutting into chips or slices	(1) Reciprocating (2) Rotary drum
Crushing machine	Crushing the skeletal structure of crude drugs, and breaking them into small pieces	Crushing roll
Pulverizer	Reducing the crude drug to powder for extraction or tablet making	Model WC-400
Drying machine	(1) Drying solid crude drugs (2) Drying extracts and other viscous fluids	(1) Track with moving plates (2) Rotary fluidized bed (3) Spray dryer

Table 4. Extraction and separation equipment

Equipment name	Function and application	Type and working principle
Multipurpose batch extraction equipment	For extraction of active principles, separation of volatile oil or concentration and recovery of solvents	Extraction kettle
Continuous extraction equipment	For continuous extraction of active principles	(1) Counter-current pressurized extractor (2) Horizontal rotary counter-current extractor
Evaporation equipment	For concentration of extracts For concentration of extracts under reduced pressure	Multiple effect evaporator (1) centrifugal film-evaporator; (2) film-evaporator with rotary scrapers
Liquid-solid separation equipment	For the clarification of fluid	Disk-bowl centrifugal

Table 5. Equipment unique to Chinese dosage forms

Equipment name	Function	Model
Honeyed bolus machine	Producing honeyed bolus of the size range 3-10 g	Model 6M-80
Wax-shell enveloping machine	Making shells, and enveloping honeyed bolus with wax-shell	Model 3600
Compression machine	Preparing compressed squares of dried infusion (12 000 pieces/h)	Model H-20
Mini-pill machine	Preparing mini-pills	
Granular infusion packing machine	Packing infusion granules in bags (50 100 bags/min)	Model BDZ-F-30
Mini-pill machine	Packing mini-pills	

Future prospects

It is clear that production of Chinese traditional remedies, including crude drugs, dosage forms and compound formulations, has made great advances since liberation. Even so, areas for further improvement still remain:

(1) It is necessary to speed up construction of facilities for cultivation and breeding. It is estimated that at present 70-80 per cent of the supply of crude drugs still depends on natural resources. Both their quality and output are uncertain. Many indispensable drugs such as musk have been in short supply for years. Therefore speeding up cultivation and artificial breeding to ensure a steady supply of these drugs is vital. Strengthening of research work and construction of production bases are called for;

(2) New formulations with specific therapeutic effects should be developed. Pharmaceutical undertakings could not flourish without R and D backing. As far as dosage forms and compound formulations are concerned, encouraging results have been obtained by analysing classical and folk recipes. Some have been simplified or found new applications. For instance, the classical recipe Dahuang-mudan-tong (rhubarb-peony decoction), has been found clinically effective in appendicitis therapy. Simplification of the recipe led to a new formulation Jinhong pian. Another example is the study of

Tianzaoheji, a folk recipe used for mid-term abortion. The original formulation consisted of four ingredients. It was simplified by biological screening to two, then to one. Finally the active principles were identified as Yuanhuacin A and B; both are polypeptides;

(3) It is necessary to adopt modern technology and equipment in production. This is the core of further development. Since Chinese traditional remedies constitute a treasure-house for investigation, much is expected to come of this.

STANDARDIZATION OF CHINESE MATERIA MEDICA

By Lou Zhi-cen*

A B S T R A C T

It is important that drugs should be uniform in quality as regards origin (authenticity), cleanliness (purity) and therapeutic potency (intrinsic quality). Such uniformity is necessary to ensure an expected result when a particular dose is prescribed and to assist pharmacists make medicinal preparations that will always be of uniform strength.

To ensure the authenticity of the drugs used, the biological and geographical origin as well as collection and preparation methods should first be ascertained by field investigation. Drugs of different origin must be assigned a suitable name in both scientific Latin and (particularly) the national language; their macroscopic and microscopic diagnostic characters should then be investigated and physico-chemical identification tests carried out.

In commerce it is seldom possible to obtain crude drugs without some adherent or admixed, innocuous foreign matter. Permissible limits of the amounts of foreign organic and mineral matter present in the drug should be established.

The therapeutic potency or content of active principle of a crude drug may be assayed biologically and with physico-chemical methods. The traditional sensory criteria for drug evaluation should be assessed scientifically since these are often used - particularly at primary collecting and buying stations in rural areas.

The methods employed in the evaluation of drug quality are discussed. The quality of medicinal preparations may also be assessed with respect to authenticity, purity and intrinsic quality; but due to the diversity of composition, state and mode of administration, there are special requirements for different types of medicinal preparations.

The prerequisite for devising methods to identify a medicinal preparation is to establish its formula and method of manufacture. To identify preparations made of powdered drugs, microscopical and physico-chemical tests should be applied; for those made from extracts or purified constitutents physico-chemical methods alone are sufficient.

To ensure the purity of a medicinal preparation, the importance of using starting materials of proven quality are

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*Professor, Faculty of Pharmacy, Beijing Medical College, Beijing.

emphasized. The harmful impurities that may be introduced into the final product during the process of manufacture should be limited and controlled.

The therapeutic potency or content of active principles in a medicinal preparation may be assayed either by methods similar to those used for the crude drug from which it is prepared or by a method specially designed for the preparation itself. The latter is particularly useful for a compound (or multi-ingredient) preparation - in order to avoid interference from the various constituents present.

The special tests related to the type of medicinal preparations include disintegration stability, variations in weight or in packing quantities, alcohol content, sterility and microbiological contamination.

If the crude drug or medicinal preparation is a recent discovery or was developed without longstanding clinical experience, a series of pharmacological and toxicological investigations should be carried out in order to ascertain its activity and safety before clinical trials are organized.

The standards proposed must be in accordance with the realities of the country concerned; all limits should be attainable, analytical methods practicable and equipment obtainable.

Crude Drugs

Drug quality has three aspects - authenticity, purity and intrinsic quality or strength. Authenticity means the correctness of biological origin (i.e. the plant or animal species and the part used). Purity means cleanliness or the amount of foreign matter present. Intrinsic quality means strength of therapeutic activity or the content of the therapeutically active constituents.

It is important that drugs should be uniform in all three aspects. Such uniformity is necessary to ensure an expected result when a particular dose is prescribed, and also to assist the pharmacist in making up pharmaceutical preparations that will always be of uniform strength.

The following discussion focuses on how to evaluate drug quality and to set up standards for crude drugs. Special regard is paid to the Chinese traditional drugs, on which the experience is chiefly based.

Drug authenticity

Authenticity is the fundamental problem in drug quality assessment. It is also the first problem to be dealt with in standardizing drug quality.

Since 1953, pharmacologists in collaboration with botanists have been making nation-wide surveys of Chinese traditional drugs with respect to their biological and geographical sources, collection and preparation, traditional

identifying methods and therapeutic uses. The results were published in a series of books. As the scientific research developed, numerous papers on Chinese traditional drugs were published in Chinese periodicals. All these works provided useful source material for standardizing Chinese crude drugs.

During the survey, it was found that there are drugs of different origin bearing the same name (in Chinese). To solve this problem, the principle of one name for each drug was adopted in the preparation of the Chinese Pharmacopoeia.

For instance, two kinds of Wu jia pi are widely used and considered effective - Cortex acanthopanacis (the root bark of Acanthopanax gracilistylus W.W. Smith, araliaceae) and Cortex periplocae (the root bark of Periploca sepium Bunge, Asclepiadaceae). After a critical study of the ancient herbals, their descriptions were found in accordance with the former and not with the latter. Therefore the name Wu jia pi was given to Cortex Acanthopanacis: Cortex Periplocae was given a new name Xiangjiapi (Xiang means fragrant) - chosen because the drug has a distinct aroma.

If a drug is neither widely used nor conforms with the description in ancient herbals, and its biological source and chemical constituents are quite different from that of the genuine drug, it is considered as false and is not permitted for use in medicine. For instance, the genuine drug Tienma is Rhizoma gastrodiae which consists of the rhizome of Gastrodia elata Blume, orchidaceae, while the roots of Cacalia tangutica (Franch.) Hand.-Mazz. (compositae), Dahlia pinnata Cav. (compositae) and Mirabilis jalapa L. (nyctaginaceae) sold in certain districts under the name of Tienma are considered false drugs.

When the biological source of the genuine drug is proved, the work on macroscopic and microscopic descriptions and physical/chemical tests for identity should be carried out.

Macroscopic descriptions include the shape, size, colour, surface and fracture characteristics, odour and taste. These characteristics are useful for identifying whole drugs, and is especially useful at collecting and buying stations in rural areas.

Microscopic descriptions include characteristics of the histological structures, cells and cell-contents visible only with the aid of a microscope. These features are especially important for identifying cut, broken or powdered drugs, for which most of the morphological diagnostic features are lost. Microscopic charecters are also useful for identifying certain whole drugs where macroscopic methods cannot provide a definite solution.

For the microscopic analysis of a whole drug, microscopic preparations of the drug in question must be prepared for examination. For most drugs, transverse sections are most useful but longitudinal sections may also be prepared where necessary. For leaves and flowers, surface preparations are essential. In addition, slides of macerated materials should be made in order to examine the details of certain cells (e.g. vessels, fibres, stone cells, oil ducts, lacticifers). To determine the nature of cell walls and cell contents (e.g. starch grains, inulin, crystals, hydroxyanthraquinones), chemical reagents may be used for carrying out microscopic reaccions. To ascertain whether starch grains are gelatinized, examination in polarized light is useful.

The microscopical analysis of c or broken drugs is similar to that for whole drugs. Because it is often d ficult to cut free-hand sections in these cases, due to the small size of the samples, the macerated or powdered material is often examined instead. For broken leaves and flowers, examination of the surface is essential.

Microscopic examination of powdered drugs is more difficult. The powdered drugs should be mounted on slides in appropriate liquids and microscopic reactions carried out. Special attention should be given to the cells and cell contents unbroken by the powdering process. Observation in polarized light is often useful.

Physico-chemical identification tests generally include simple chemical qualitative reactions, examination with ultra violet light, microsublimation and various chromatography methods. Thin-layer chromatography is especially useful and because of its simplicity and rapidity, higher sensitivity and wide applicability the method is now widely used.

Purity

Crude drugs are required to be as free as possible from mould, insects and other animal contamination, including animal excreta. They must also show no abnormal odour, discoloration, sliminess or other evidence of deterioration.

In commerce it is seldom possible to obtain crude drugs that are completely free of adherent or admixed innocuous foreign matter. No poisonous, dangerous or otherwise noxious foreign matter or residue may be present, however.

Foreign matter, if present in a significant amount not only lowers the therapeutic effect of the drug, but may also cause unpredictable results in preparation or administration. It is therefore necessary to set limits on the amount of foreign matter present. In setting such limits, drug samples collected and prepared with reasonable care should be taken as a reference standard.

Foreign matter may be organic or mineral. Foreign organic matter may also be further divided into two categories:

(1) Parts of the organism or organisms from which the drug is derived, other than the parts named in the definition and description or for which a limit is specified in the monograph - for example, the stalks or small branches present in cloves;

(2) Organisms or parts or products of organisms, other than those named in the definition and description - for example, weeds present in certain herbs.

Foreign organic matter in whole, cut or broken drugs, is generally detected by inspection with the naked eye, with the aid of a magnifying lens, or by using a suitable sieve. Physical, chemical or microscopic tests may be necessary where the foreign matter closely resembles the drug.

The qualitative detection of foreign organic matter in powdered drugs can be done simultaneously with microscopic and chemical identity tests.

The quantitative determination of foreign organic matter in a powdered drug is a more difficult problem. The lycopodium method designed by T.E. Wallis seems useful for admixtures of the following: (1) material containing starch grains mixed with that containing none; (2) material containing fibres or stone cells mixed with that containing none; (3) material containing epidermis mixed with that containing none; and (4) mixed spores or pollen grains of different plant species. This method requires highly skillful techniques, however.

Foreign mineral matter includes stones, sand, soil and dust. Soil and dust are firmly attached to the drug surface but sand and stones are easily separable. The separable portion of mineral matter may be determined by sifting and weighing. The portion of mineral matter firmly attached is usually determined by ash and acid-insoluble ash contents. The ash of drugs includes the physiological ash derived from mineral salts naturally present in the plant or animal tissue and non-physiological ash derived from foreign matter, especially soil and sand adhering to the surface.

It is clear that only the non-physiological ash has to be limited. Due to the fact that physiological ash of crude drugs is usually only a small percentage and is quite constant for each species, total ash may be taken as an indication of the extent of foreign matter present. But in certain cases, however, the physiological ash varies with different samples of the same drug due to the presence of large and variable quantities of calcium oxalate (such as in rhubarb). Determination of total ash would therefore not be a reliable indication of the extent of foreign mineral matter present. It is necessary in these cases to determine the acid-insoluble ash, which is a measure of the amount of silica, especially sand and siliceous earth, present. In this case, acid-insoluble ash is a better indication of the amount of foreign mineral matter present.

Excessive amounts of water present in a crude drug not only increase the weight of the drug but also induce mold growth and promote drug deterioration. It is therefore necessary to limit it. The water content of crude drugs is usually determined by gravimetric methods (loss on drying) but azeotropic methods (e.g. toluene distillation) are necessary for drugs containing volatile constituents.

Intrinsic quality or strength

The intrinsic quality or strength of a crude drug chiefly depends on its content of therapeutically active constituents and on many factors, such as breeding, culture, collection, preparation, drying and storage. Homogeneity and uniformity with different drug samples is therefore impossible - drugs derived from wild plants especially so. The determination of intrinsic quality and standardization of the content of active constituents is thus especially important.

In the old days, the quality of crude drugs were judged by sensory methods, which are not only simple, but also in many cases, rational. For instance, Cortex cinnamomi and Herba menthae with a strong aroma, Rhizoma coptidis and Cortex phellodendri with a deep yellow colour and, Radix

glycyrrhieae with a sweet taste are considered drugs of good quality. But the degree of colour lightness and strength of odour and taste were all judged subjectively and the result varied from person to person and even from time to time for the same person. These methods can only give a rough assessment of drug quality and cannot yield accurate results. Nevertheless due to the simplicity of these methods, they may be used as a preliminary and rough guide to drug quality and are especially suitable for the primary collecting and buying stations situated in rural areas.

However, these traditional criteria for drug quality evaluation may also give information contradictory to scientific findings. For instance, the Radix puerariae derived from Pueraria thomsonii cultivated in south China is traditionally considered as of good quality due to its "white colour, compactness and mealy texture". In contrast, that derived from Pueraria lobata grown wild in north China is considered poor quality due to its "yellowish colour, looseness and fibrous texture". Scientific research on the contents of their therapeutically active constituents in recent years showed that the reverse is true.

It is clear, therefore, that the suitability of traditional quality criteria should be proved by scientific investigation. Some of these criteria and methods, after appropriate refinement, may become reliable biological criteria and methods of assay, such as the biological assay of bitterness specified in some of the European pharmacopoeias for certain bitter drugs. Physico-chemical methods are certainly the methods of choice for the quantitative determination of active principles of crude drugs. These methods can give much more accurate results and have developed very rapidly in recent decades. They range from the classical gravimetric, volumetric and colorimetric methods to various chromatographic, and spectrometric techniques, as well as a combination of the two; from the determination of the total content of a group of compounds (such as total alkaloid, total flavonoids etc.) to the content of individual compounds of a chemical group. When the pharmacological activity of these individual compounds are fully and quantitatively elucidated, the evaluation of drug quality will see great progress due to employment of these fine assay methods.

Biological assay methods play an important role when a new method of physico-chemical assay is being sought. In some cases they can serve as a beacon-light in the investigation process. For instance, the biological assay of cardiac drugs helped the development of physico-chemical method of assaying drugs containing cardiac glycosides; improvements in the biological assay of vegetable purgatives prompted the development of physico-chemical methods for the assay of rhubarb, senna and cascara. In order to develop fine physico-chemical assay methods, it now seems necessary to emphasise biological assay methods that require only a small amount of test sample. This permits individual compounds isolated in milligrams to be assayed for their activity. Furthermore, for a number of drugs, no reliable physico-chemical assay method is available, and biological methods of assay are therefore still essential. Examples are the determination of haemolytic activity of certain saponin-containing drugs and the determination of bitterness for certain bitter drugs.

The determination of volatile oil is also important for drugs containing volatile oil as their therapeutically active constituent. It should be noted, however, that the composition of volatile oil present in a crude drug is

easily influenced by intrinsic and extrinsic factors. For instance, two samples of Asarum sieboldi obtained from different sources were assayed for the chemical constituent of the volatile oil. It was found that one sample contained methyleugenol and the other, safrole, as the chief constituent of the oil. It is therefore necessary to identify and determine the content of the chief constituent of the volatile oil present. Gas chromatography is an important tool for solving this problem.

The active principles of many Chinese traditional drugs have not yet been fully elucidated. For these drugs, it is presently only possible to determine the content of extractives. For this, the powdered sample is extracted with a measured volume of water, ether or alcohol of appropriate strength and filtered. An aliquot of the filtrate is evaporated, dried and weighed. Following the elucidation of active principles, these methods will be gradually substituted by more accurate physico-chemical assay methods.

The establishment of drug assay methods will not only promote evaluation and standardization of the quality of crude drugs and their preparations, but also prompt investigation of methods for improving the quality and production of crude drugs and their medicinal preparations.

Medicinal preparations

Crude drugs may be converted into various types of medicinal preparations to meet different therapeutic requirements. The preparations now widely used in China include pills, tablets, granules, extracts, ointments, plasters, powders and injections. Traditional pills and powders are made from powdered drugs; tablets, granules, ointments and newer types of pills are mostly made from extracts or purified extracts. Injections are made from purified extract or pure active constituents isolated from the drug.

Since medicinal preparations are used by the patient directly, the importance of uniformity of quality cannot be over-emphasized. The quality of medicinal preparations may also be evaluated with respect to authenticity, purity and intrinsic quality, but due to the diversity of composition, state and administration method, there are special requirements for different types of medicinal preparations. These are briefly outlined below.

Authenticity

The prerequisite for designing methods to identify a medicinal preparation is to fix its formula and method of preparation. Traditional pills and powders made of powdered drugs can be identified by means of microscopic and physico-chemical tests. To identify preparations made of extracts or purified constituents, physico-chemical methods alone are useful.

Simple preparations (i.e. preparations made from a single drug or constituent) can usually be identified with the method and criteria prescribed for the corresponding crude drug. Identification of the various ingredients present in a compound preparation is much more complicated. Due to the interference of the ingredients, their microscopical identification requires both highly skillful techniques and mastery of the diagnostic features of powdered drugs. Regarding the physico-chemical identity tests, if the constituents are too complicated, they may be isolated into several groups, for instance, by extraction with organic solvents at different pH. The chief

constituents in each extract are then separately identified by thin-layer chromatography. Their ultra-violet spectra, infra-red spectra, gas-chromatograms or thermofracto thin-layer chromatograms may also be prepared and compared (as with finger prints) with those of the authentic samples.

Purity

If the foreign matter is present in fairly large amounts, it is easily detected during authenticity identification. If it is present in small quantities, its detection may be very difficult. This is especially the case with compound preparations. The manufacturers are therefore required only to use starting materials of proven quality and to keep analytical reports as well as records of the quantities of starting materials use and production details.

In addition, there are harmful impurities that may be introduced into the final preparation during the manufacturing process; these also have to be limited and controlled. For instance, there are limit tests for heavy metals in extracts, for freedom from acetone, isopropanol and tertiary butanol in alcohol-containing preparations and for solubility or insoluble matter in soluble granules and aqueous extract.

Strength or potency

The fundamental criterion of the strength of medicinal preparations, therapeutical potency, chiefly depends on the content of therapeutically active constituents. This may be determined by methods similar to those prescribed for the crude drug. However, the method used for crude drugs usually have to be modified or even redesigned in order to avoid interference from different constituents present in the compound preparation. Therefore, the determination of each active principle in a compound preparation is a problem that requires detailed investigation.

Factors related to the type of medicinal preparation

(1) Disintegration test. To ensure rapid disintegration of tablets, pills and capsules after oral administration (so that the active principle may be absorbed from the stomach or intestine) it is necessary to set up a time limit within which the sample preparation is required to disintegrate or dissolve completely when tested by a specified method. The time limit for tablets is usually 15 minutes, for sugar-coated tablets and pills made of powdered drugs, 1 hour; for pills or tablets made from extracts, 2 hours.

(2) Variation in weight and in packing quantities. To ensure dosage uniformity it is necessary to set up a limit for weight variations of tablets and pills, and a limit for variations in the amount of material packed in the dosage container. The latter limit is applicable to capsules, granules, powders and sterile powders used for injection.

(3) Alcohol content. Tinctures, liquid extracts and medicated wines that contain alcohol should have their alcohol content specified and determined. Otherwise variations of alcohol content will affect the solubility of active principle present. The alcohol content specified for these preparations is usually slightly lower than that of the menstruum used, thus making allowance for reasonable change of alcohol concentration during manufacture and storage.

(4) Test for sterility and microbiological contamination. In order to ensure safe administration, preparations for parenteral injections are required to comply with the test for sterility. It is suggested in the International Pharmacopoeia (second edition, 1967) that for other pharmaceutical preparations the extent of microbiological contamination should be no greater than that permitted for foods under the law of the country concerned.

(5) Sensory characteristics. These characteristics affect not only the external appearance of the preparation but also their quality or therapeutic effect. Some standardization of sensory characteristic is therefore necessary - for example, the particle size in powders, and the integrity, uniformity, surface brightness and cleanliness of tablets, capsules and pills. Extracts should be required to preserve the odour and taste of the crude drugs from which they are prepared.

Other considerations

So far the discussion has focussed on the quality and standardization of crude drugs and their medicinal preparations that have been used traditionally or proved to be efficacious and safe by scientific investigation. If a new crude drug or medicinal preparation is discovered or designed, a series of pharmacological and toxicological investigations must be carried out in order to ascertain its efficacy and safety before clinical trials are organized. And only at this stage, can the work on quality evaluation and standardization be started.

For the standardization of a crude drug, sufficient quantity of representative samples must be collected and the authenticity of their biological origin proved. The biological origin of samples taken from commercial drugs are not always reliable, they should be checked with the reference standard sample taken from organisms of proved identity.

For standardization of a medicinal preparation, emphasis should be firstly on the quality of starting materials, the reasonableness of manufacturing process and the strictness in carrying it out. It is necessary to check the analytical record and batch manufacturing records and collect representative samples of as many batches of the product as possible. The items to be standardized are then proposed according to the type and composition of the preparation concerned. The analytical methods are designed and investigated, and finally, a preliminary draft of the quality standard of the drug or preparation is prepared for further discussion, revision and approval.

It should be noted that the standards proposed should be in accordance with the reality of the country concerned. All limits should be attainable, analytical methods practicable and equipment obtainable. The golden rule for selecting analytical methods is accuracy, rapidity, simplicity, and cheapness.

TRADITIONAL PHARMACOPOEIAS REVISITED

By the UNIDO secretariat

Introduction

The story of man's life on earth is dominated by his symbiotic relationship with the plant kingdom. It was from plants that primitive man derived materials for food and drink, clothing and shelter, health, happiness and general well being. In the quest for drugs to conquer disease man came across plants with healing properties, and doubtless some of them first tried were toxic or had unpleasant reactions. However over the many millennia there has evolved in every culture and region of the globe groups of plants that are considered safe and efficacious; many are in use even today for curative purposes. Similarly, there evolved a further group of plants, aromatic by nature, from which are derived perfumery and flavour-giving substances that have a wide variety of uses in our industrialized world.

Almost all drugs commonly used today, fall into three categories:

(a) Drugs derived from natural sources - animal, vegetable and mineral;

(b) Synthetic drugs: totally synthetic, partially synthetic; modified plant constituents;

(c) Drugs obtained by microbial action.

The synthetic drugs are of comparatively recent origin: the synthetic drug industry came about only after the massive developments in organic chemistry that followed the Second World War.

Drugs derived from natural sources have indeed dominated all but the comparatively infinitesimal part of time represented by four or five modern decades. It is therefore highly relevant that, given the recent emergence of a large part of the globe with aspirations and hopes of a better life, there should commence a trend to re-examining the traditional cures of the past, which are to a very large extent derived from plants. This does not in any way represent a movement backwards. But it is very much a revisit of old traditions to examine what the application of modern science and technology to the treasures of the past could come up with.

Problems, prospects and practices in producing plant-derived pharmaceuticals

The problems facing developing countries in processing pharmaceuticals for use in their health-care systems are enormous and sometimes intractable. The foreign exchange resources of many countries do not permit the acquisition of even their basic needs in essential drugs. One major way in which this situation may be met is in the development of pharmaceuticals derived from plants used in traditional systems of medicine. In almost all countries of the world where traditional systems of medicines are practised, where the main therapeutic agents are derived from plants, the drugs are prepared directly from the plant material using one of several simple methods:

Extraction with cold or hot water

Crushing and compressing of materials which are generally succulent

Pulverising and admixture with oils

Such simple methodology raises several questions:

Has the plant species been correctly authenticated?

Is the method of preparation used, consistent with the prescribed one?

Are the dosages employed in accordance with prescription?

Is the raw material used of approved quality?

Standardized procedures and techniques in the preparation of such extracts would be a first step in the utilization of plant-derived pharmaceuticals in developing countries. In order to ensure the wide acceptance of extracts by health authorities in both developing and developed countries it would be necessary to ensure the following:

Authenticated plant material of uniform quality

Strict conformity to prescribed/predetermined methods of extraction

Rigid control of quality during all stages of production and in the final products

During the past ten years there have been many instances where extracts of drugs produced from plants used in the traditional pharmacopoeias of developing countries have been processed by modern technological means [1]. Many such drugs have been successfully introduced into use in developed countries, even in Europe (table 1).

In addition there are many new extracts that, on account of their long standing inclusion in traditional pharmacopoeias and the results of recent research utilizing established scientific norms, are receiving close attention. Examples include:

Mormodica charantia	Treatment of diabetes
Commifora mukul	Useful in reducing arteriosclerotic syndromes
Anethum graveolens	Digestive problems.

There are many others with promising clinical effects that can be manufactured industrially as dosage forms for the use of developing as well as developed countries (table 2).

The plants in table 2 are only some examples where the technology for producing extracts or active ingredients is already known - known invariably to commercial drug firms in the industrialized countries. In several instances there are patents covering the extraction process that could legally hinder the utilization of a plant for therapeutic preparations even though the plant itself is grown in a developing region.

Table 1. Extracts from plants listed in traditional pharmacopoeias now available as modern, industrially-processed pharmaceutical preparations - (some examples)

Crude drug	Use in treatment
Prurius africana (Hook)Kalk.	Adenoma of the prostrate (using the anti-testosterone activity of some of its constituents)
Centella asiatica	Syndromes requiring a non-steroidal anti-inflammatory healing agent
Siliabum marianum	Normalization of liver dysfunctions
Valeriana wallichi	Non-sedative tranquillization
Panax ginseng (C.A. Meyer)	Anti-stress agent
Anarcardium occidentale	Anti-amoebic agent Anti-hypertensive agent
Rhamnus purstriana D.C.	Laxative action
Rhamnus frangula L	Laxative action
Vaccinium myrtillus L.	In opthalmology for treatment of hemeralopia, capillary diseases, circulatory disorders
Ruscus aculeatus L.	Anti-inflammatory drug haemorrhoids, varicose veins

Table 2. Plant species currently used in traditional medical therapy and warranting industrial processing

Clinical use	Plant source
Tapeworm	Cucurbita maxima Duch. (seeds) Cucurbita pepol. (seeds) Punica granatum L. (fresh bark)
Anti-schistosomiasis (bilharzioses)	Securinega virosa Baill. (leaves, twigs) Diatium dinklagei Harms. (leaves) Pargularia extensa N.E.Br. (latex) Cnestis ferruginea DC (roots) Combretum glutinosum Perr. (fruits) Tylostemon manii Stapf. (fruits) Borreiria verticillata G.F. Mey (whole plant) Zizyphus mucronata Willd. (roots) Hibiscus furcatus Roxb. (leafy stems) Ageratum conyzoides L. (aerial parts) Cochlospermum tinctorium A. Rich. (rhyzomes)
Other anti-helmintic agents	Securidaca longipendanculata (roots) Ploygala senega (roots) Phytolacca dodecandra (roots) Chenopodium ambrosoides (aerial parts) Pooygonum senegalensis (leaves)
Anti-amoebic agents	Hollarhena floribunda (seed or roots) Anarcardium occidentale (kernal) Euphorbia hirta (whole plant) Simaruba glauca (bark)
Anti-malarial agents	Mitragyna spp. Corynanthe pachycoras Nauclea latifolia Morinda citrifolia Crossopterix febrifuga Khaya senegalensis Guiera senegalensis Combretum micranthum
Anti-microbial agents	Several species of Flacourtaceae centella asiatica
Anti-leucodermic agents	Heracleum spp.

Source: J. Kerharo [3].

Accordingly, there is no question but that industrial production of drugs from plants must, for economic as well as reasons of health-care practice, receive high priority in modern pharmaceutical R and D policy (particularly in developing countries). The technology must thereby be evolved for processing these plants into drug forms. Much of the R and D effort during the past few decades has been carried out in the industrialized countries using plant material gathered from developing countries. It has therefore not benefitted the country in which the plant was originally located.

Such exploitation invariably uses the following sequence:

Verification of ethnomedical information

Collection of plant material

Chemical studies

Studies on Bioactivtity/toxicity etc.

Isolation of active ingredients

Synthesis of appropriate analogues

Marketing of synthetically produced compounds.

Examples of this type of activity range from the production of quinine in Europe (from cinchona bark produced in Africa and south America) to the United States National Cancer Institute's recent screening of African plants for anti-tumour agents. The plant material is more often than not exported to the industrialized country in the crude form.

As fully recognized by UNIDO [2], this sequence has not benefitted the developing countries in any way. Generally, biologically interesting compounds have been isolated and their chemical structures elucidated. Sometimes their pharmacological activities have also been systematically studied; where promising results have been forthcoming in a very small percentage of compounds, the natural products themselves or analogues have been prepared synthetically. Such synthetic products after rigorous evaluation are marketed by drug firms, and the poor developing countries pay dearly for their acquisition.

The question is clearly begged: why cannot the original plant be systematically cultivated and a drug from it processed in the country or countries in which it is grown? Must the discovery of new drugs from plants invariably end by sacrificing the plant-drug to the synthetic process? Clearly, an alternative approach to drug development should be considered, one that would directly and speedily benefit the developing countries.

There is a powerful case for a methodology where the ethnomedical preparations are simulated so that they are equally effective and can be produced using modern technologies. UNIDO programmes have therefore been directly towards this end.

Another question to be considered is the use in traditional systems of medicine of plant preparations where more often than not several plant species are included as a single prescription for a given disease. It is contended that in such "polyprescriptions" the individual effect of the plant species that is specific for a particular disease is rendered more effective and would have less harmful side effects than when it is used by itself. Therefore to

test the plants individually would clearly render the results of limited value. There are instances [4] where it has been proven that the extract of a whole plant made according to ethnomedical prescription is more effective and less toxic than an individual constituent in it. Hence much of the previous work on evaluating plant medicines suffers in the light of this consideration.

It is therefore neccessary to reconsider the approaches to drug development from plants. The expense, for instance, of isolating a pure constituent does not make sense if the specificity displayed by the extract is lost; it would therefore not be justified on therapeutic grounds. Furthermore techniques are now available [5, 6] for manufacturing both solid and liquid pharmaceutical preparations utilizing plant-extracts without jeopardizing their efficacy, and indeed enhancing their stability. UNIDO programmes have taken this into account.

The general trend to isolate pure compounds from plants is dictated by the following considerations:

the possible discovery of new structural types with interesting biological activities

the facility with which pure compounds can be pharmacologically assessed, and standardized dosage forms prepared

the stringent requirements in terms of toxicology tests and standardization

While the first two of these are justified on scientific grounds (while also enabling methods to be devised for the quality assessment of products based on total extracts); there are many reservations regarding the third. The World Health Organization and many national drug regulatory authorities demand the same requirements for toxicological and teratogenic assessment of drugs produced from plants as for synthetically produced drugs. While considerable caution is justified in the case of drugs from the synthetic process, the same cannot hold for simulated preparations derived from plants that people have used for generations. More realistic criteria for them must surely be evolved. For example conducting animal experiments on preparations of plants such as Coriandrum sativum, Centella asiatica, or Momordica charantia and the like, which are routinely used by people (and have been for several millenia) as drugs and even as food items, would sound as absurd to people in Africa, Asia and Latin America, as conducting similar experiments on carrots, lettuce and cabbage would to people in Europe.

There are many who still believe that strict quality control of multiple constituent plant extracts is not within the realm of possibility. Admittedly such quality control methods are not as simple as when only pure compounds are involved - but they are possible. Recent publications document a host of such methods [5-10]; for example modern analytical methods such as infrared and ultraviolet spectroscopy, gas-liquid chromatography and high-performance liquid chromatography are most effectively used in the quality control of drugs derived from plant extracts.

Industrial processing to serve the needs of developing countries

There are several approaches [11-14] to the utilization of plants for the industrial production of pharmaceuticals. However, an approach characterized by service to developing countries would be based securely on the systematic

cultivation of the plant species in developing countries and would seek to encourage manufacture of such pharmaceutical formulations within the developing countries themselves.

Considering traditional as well as current practices, the utilization of medicinal plants today may take one or other of the following forms:

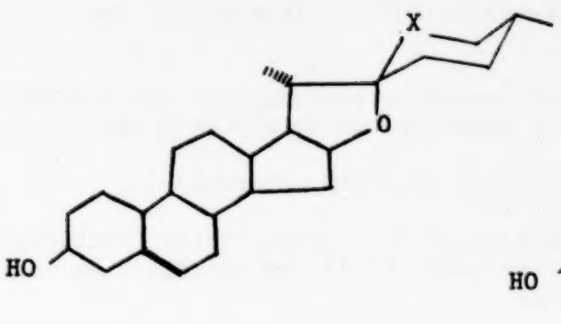
(a)	Direct use:	Use of fresh or dried material
(b)	Extraction:	Preparation of decoctions, teas, tinctures and galenicals; pills and tablets from total extracts
(c)	Isolation of constituents:	As raw material for the extraction and isolation of pure constituents or isolates for therapeutic use
(d)	Synthetic intermediates:	As raw materials for isolating intermediates for synthetic production

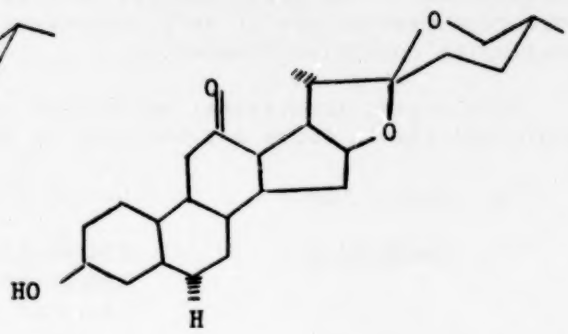
Direct use of plant material is a feature of all systems of traditional medicine, not only in developing areas but also in Europe where today there is a considerable resurgence of interest in plant-derived medicines. The production of extracts, tinctures, teas, galenicals, and other forms is also common in many countries, albeit in varying degrees of sophistication. China, for instance, has pioneered the utilization of modern scientific technology in the preparation of plant-derived medicines and in the integration of modern technologies with ethnomedical knowledge and its application [14].

The isolation of constituents, their purification and preparation into drug forms and their biological evaluation on animal species followed by clinical trials of varying degrees of exposure to humans has been the preferred pathway of drug development followed in the industrialized world. This methodology not only requires high-cost, sophisticated technology - not available in most developing countries - but also involves animal experiments for toxicology and teratology with enormous outlays in funds. The time frame starting from the availability of pure compounds to the development of drug forms licenced for clinical usage is of the order of 6 to 15 years. Poor developing nations that most require the drugs can neither afford the time nor the funds for such exercises.

The fourth use category, namely production of intermediates for the synthesis of drugs can however be of some use to developing countries. Two cases exemplify the possiblity.

The first is the preparation from plants of intermediates in the production of corticosteroids [15]. These were originally obtained by extraction from animal sources and later by partial synthesis from cholesterol. In the 1940s, R.E. Marker working in Mexico found that some steroidal sapogenins obtained from plants, in particular diosgenin from Discorea spp. could be utilized for the preparation of certain corticosteroids. This included cortisone and prednisone (see figure 1) which were already widely used. Development of synthetic methods by C. Djerassi also enabled the production of a practical oral contraceptive utilizing diosgenin-type compounds thereby increasing the international market for such steroidal intermediates considerably.



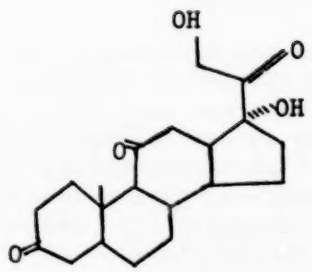


X = -O-: Diosgenin
X = -NH- Solasodine

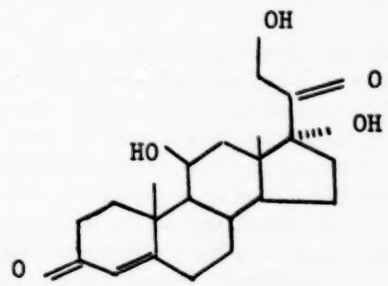
Hecogenin

Several stages

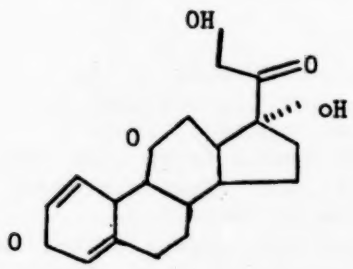
Corticosteroids



Cortisone



Hydrocortisone

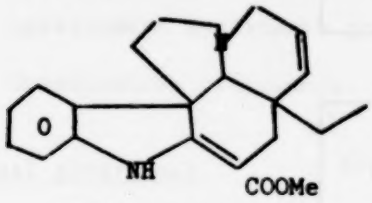


Prednisone

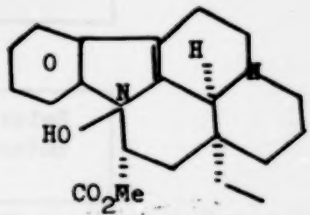
Figure 1. Structures of plant-derived steroidal sapogenins and their derivatives

As a result, various species of dioscorea such as D. deltoidea Wall and D. floribunda are now being cultivated in countries such as Mexico and India for production of diosgenin. Similarly the steroidal alkaloids, like solasodine (the nitrogen analogue of diosgenin) are a group of compounds present in the Solanum spp. These are an attractive source of steroids for drugs and can be grown in many developing countries.

Another example is tabersonine,



Tabersonine



Vincamine

a principal constituent of the African species Voacanga africana and Voacanga thoursii. Tabersonine can be synthetically converted to the oncolytic drug vincamine, which although the most biologically significant alkaloid of Vinca minor, is present in only small amounts in the Vinca spp. Its production from tabersonine is a commercially viable proposition and there are several patents covering its synthetic conversion. Production of tabersonine from Voacanga spp. is also an attractive proposition for many African countries, although its conversion synthetically to vincamine requires fairly sophisticated synthetic capability.

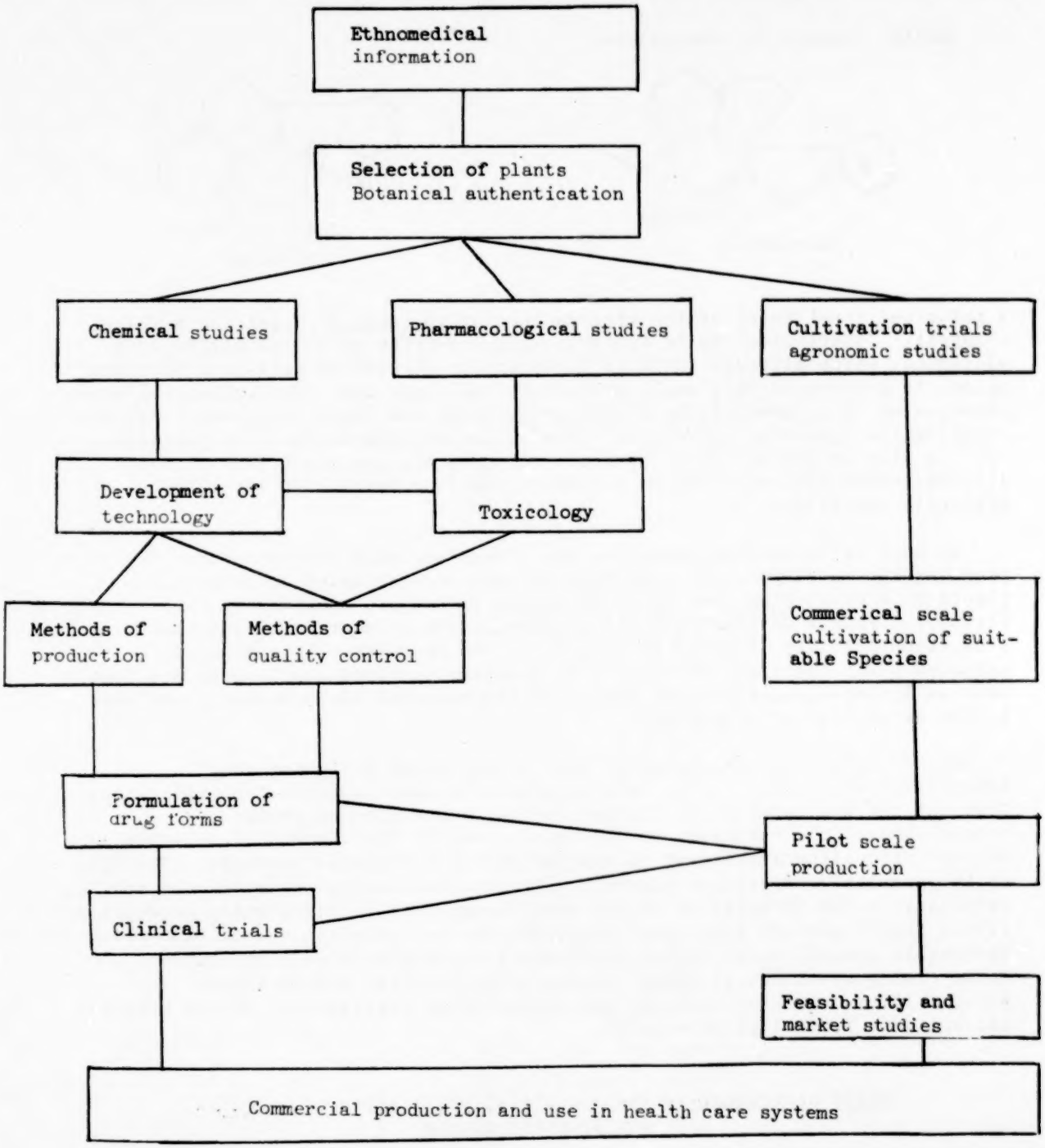
It must be recognized therefore that there are many considerations in planning the development of a pharmaceutical industry based on medicinal plants in a developing country. The stages needed are outlined in the figure 2. From a developing country viewpoint it is most important that production activity is based on systematic and cropwise cultivation of selected plant species. Dependence on spontaneous flora can lead to problems such as inconsistencies in the supply of raw material for processing and even to the extinction of a species.

Accordingly, agronomic studies must be initiated following the identification, authentication and selection of plant species for utilization. Chemical and pharmacological studies logically precede the choice and acquisition of the necessary technologies, and the development of suitable methods of quality assessment of raw material and finished products. The data on the chemical composition together with the pharmacological responses are necessary in the formulation of suitable dosage forms. Pilot-scale production trials should precede both feasibility studies and clinical trials, for which reasonable quantities of standardized material should be made available. Commercial production can commence only after quality, efficacy and acceptability have been assessed and a continuing availability of raw material and suitable technology is assured.

UNIDO programmes in the industrial utilization of medicinal and aromatic plants

UNIDO programmes in the area of medicinal and aromatic plants [2] in the past five years have tended to accent firstly the aspect of industrial utilization. This is in keeping the UNIDO mandate "to promote and accelerate

Figure 2. Stages in planning the development of a pharmaceutical industry



the industrialization of the developing countries". Secondly, all UNIDO programmes have been developed with the problems and concerns of developing countries discussed previously in mind. Broadly these programmes could be divided into four categories:

(a) Promotional programmes;

(b) Exploratory programmes;

(c) Development assistance programmes;

(d) Consultative programmes.

Promotional programmes

The main promotional programme took the form of a unique exploratory mission by a mobile unit organized by UNIDO with the collaboration of the Joint UNIDO-Romania Centre, Bucharest. This was confined to the Least Developed Countries of Asia and Africa.

The mobile unit itself consisted of two four-wheel-drive vehicles fitted out with instrumentation and laboratory facilities to enable the five-man crew of Romanian scientists and technologists to carry out basic laboratory screening tests and semi-pilot scale operations on plant materials. The mobile unit first visited Afghanistan and Nepal, spending a total of five months from departure and return to Bucharest. The African phase included visits to Botswana, Burundi, Rwanda, Sudan and the United Republic of Tanzania. In the course of an arduous and rewarding project the team's accomplishments included:

(a) Gathering data on the spontaneous flora of each country visited;

(b) Listing and authenticating important species of medicinal plants growing in each country;

(c) Demonstrating methodologies of field botany, phytochemical screening and pilot scale methods of extraction and distillation;

(d) Establishing liaison with interested institutions in each country visited and with local scientific and technological personnel.

The success of this exploratory mission and the interest it generated may be gauged by the fact that UNIDO has already been able to initiate full-fledged technical assistance programmes in Botswana, Nepal and Rwanda on the production of pharmaceuticals from plants. In the next two years projects in Afghanistan and the United Republic of Tanzania will also commence. The mobile unit mission, which cost around $80,000, could be considered a success in these terms alone.

Exploratory programmes

The exploratory programmes of UNIDO are considered a necessary prerequisite for the initiation of long-term technical assistance programmes. The production of pharmaceuticals from plants on an industrial or semi-commercial scale becomes a viable proposition only if the raw material for processing is available continuously and in the required quantitites. For this purpose, it is necessary to understand that total dependence on the

spontaneous flora will eventually be detrimental to both industrial prospects and the environment. Placing the plant species selected for processing on a crop basis, is thus a prime requirement.

Accordingly, UNIDO's exploratory programmes have taken the following forms:

(a) Economic mapping of the spontaneous flora;

(b) General assessment of the plant resources - forest flora as well as flora cultivated for utilization in pharmaceutical production.

The method of economic mapping devised by the Romanian scientist Ovidou Bojor [16] gives an idea of the number of plant species that could be profitably utilized and their relative abundance in a given geographic region. It was successfully used to assess, with a view to industrial processing, the spontaneous flora of Afghanistan and Nepal. In particular, the technical assistance programme in Nepal will take into account the results of economic mapping for both utilization of forest flora and selection of plant species for cultivation on a crop basis for industrial processing into pharmaceuticals.

Other assessment programmes of a general nature have preceeded the assistance projects in Guinea, the Republic of Cameroon and Rwanda. Several such programmes designed to assess qualitatively the flora for suitability for initiating pharmaceutical production are now underway.

Technical assistance programmes

UNIDO technical assistance programmes in this area involve transfer of technology for producing pharmaceuticals from medicinal and aromatic plants to the country concerned. This means provision of technology at one or more points in the series of operations represented in figure 3.

In the past UNIDO has provided several countries in Asia, Africa and Latin America and the Caribbean with assistance in:

assessing plant resource potential

cultivation technology for industrial processing

processing technology

analysis and quality control methodology

marketing and management of production

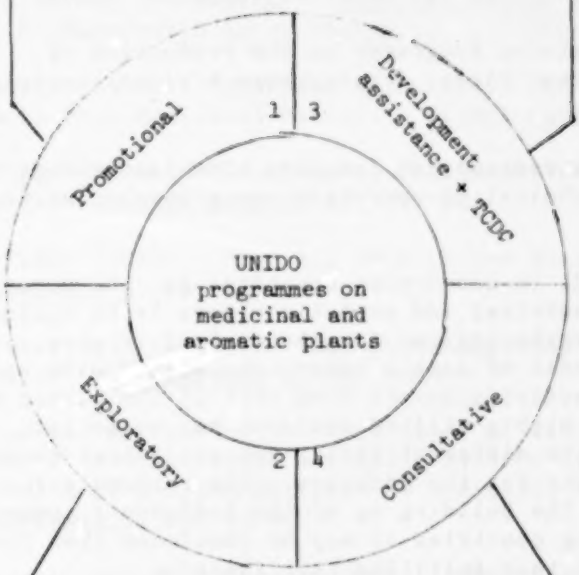
The projects in Nepal and Rwanda are examples where UNIDO was engaged in strengthening the resources and the capacity of local R and D institutions - the Royal Drugs Research Laboratory, Kathmandu and the Centre Universitaire de Recherche sur la Pharmacopie et la Médecine de Butare, Rwanda - UNIDO provides the experts and assists in the selection, evaluation and procurement of equipment for production and analytical quality control. UNIDO experts work in collaboration with national counterparts and the programme is jointly executed as a concerted effort to develop the industry within each country. Several other smaller UNIDO projects have been or are now being executed where UNIDO assistance helps in developing agronomic expertise, analytical facilities, research and training facilities, with the ultimate aim of utilizing the plant resources for pharmacological production. These include projects in Botswana, Guinea, the Republic of Cameroon and Upper Volta.

Figure 3. UNIDO programmes on the industrial utilization of medicinal and aromatic plants

Mobile Unit Exploratory Missions:
Afghanistan
Burundi
Nepal
Rwanda
Sudan
United Republic of Tanzania

Technical assistance in production of cinnamon oil Sri Lanka-Seychelles

- Strengthening of the Royal Drugs Research Laboratory (Nepal)
- Assistance to Centre for Research in Traditional Medicine (Rwanda)
- Inaugural Assistance for the Central Analytical Laboratory (Guinea)
- Assistance to the Centre for Studies on medicinal plants (the Republic of Cameroon)
- Assistance in the production of plant pharmaceuticals (United Republic of Tanzania, Upper Volta)



- Assessment of spontaneous flora (Afghanistan, Algeria, Guinea-Bissau, Nepal, Togo)
- Economic mapping of medicinal and aromatic plants (Nepal)
- Prospects for cultivation of medicinal plants for industry (Nepal, the Republic of Cameroon, Rwanda)
- Technical feasibility assessment (Arab States, Botswana, Kenya, Lebanon)

- Technical meetings and workshops: Production of Drugs from Medicinal Plants (Lucknow, 1980)
- In-Plant Group Training Programme (Bucharest, 1980)
- Workshop on Essential Oil Industry (Lucknow, 1981)
- In-Plant Group Training Programme (Bucharest, 1982)
- Workshop on Traditional Medicine (Beijing, 1982)

Similar projects are now being developed by UNIDO in other countries of Asia, Africa and Latin America. Hopefully these will materialize into technical programmes reaching the execution stage in the near future.

Consultative programmes

Recent UNIDO consultative programmes featured the following main events:

(a) A technical consultation on the Production of Drugs from Medicinal Plants in Developing Countries (Lucknow, India, 1978);

(b) In-Plant Group Training Programme in the Field of Medicinal Plants (anglophone countries, Bucharest, 1980);

(c) Workshop on the Essential Oil Industry (Lucknow, India, 1981);

(d) In-Plant Group Training Programme on the Production of Pharmaceuticals from Medicinal Plants (francophone African countries, Bucharest, 1982);

(e) Workshop on the Pharmaceutical Industry (Combined Modern-Traditional Pharmacy) for Promoting Technical Co-operation among Developing Countries (Beijing, 1982).

One of the crucial needs in developing countries for the purpose of inaugurating projects on medicinal and aromatic plants is to build up an indigenous scientific and technological competence in this area. The multidisciplinary requirements of such a competence span a wide spectrum of subject areas and involve activity levels from that of the farmer who cultivates the crop to the highly skilled professional scientist. The successful interaction of the different skills and activities generates the infra-structural requirements for the industry. The rationale for UNIDO consultation programmes is the building up of the indigenous competence: from reactions of many developing countries it may be concluded that the UNIDO programmes have indeed more than fulfilled that function.

Training of personnel is a most important aspect of the transfer of technology. In the context of UNIDO programmes there are many constraints, however - such as the dearth in several countries of suitable personnel capable of undertaking training and the non-availability of tailor-made training schemes for the activities concerned. However over the years UNIDO has given highest priority to building national capabilities in all the multidisciplinary aspects of the industry.

In conclusion, it will be seen that, although there is nowadays a strong interest in medicinal plants and their possibilities of inexpensively providing useful drugs for the world's most needy, what is still needed is a concerted global effort to that end. Such an effort calls for long-term planning by all United Nations and other agencies interested in the subject and, more especially, long-term availability of funds. UNIDO's efforts so far will hopefully serve as a nucleus for a future global effort in assisting the developing world build a pharmaceutical industry based on indigenous raw materials - with a maximum benefit to a greater part of the world.

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